"THE STUDY OF THE EXPRESSION OF MUC-1 IN GASTRIC CARCINOMAS AND ITS CORRELATION WITH THE CLINICO-PATHOLOGICAL VARIABLES"

Dissertation submitted in partial fulfilment of the requirements for the degree of

M.D. (PATHOLOGY)

BRANCH - III

INSTITUTE OF PATHOLOGY

MADRAS MEDICAL COLLEGE

CHENNAI – 600 003

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

APRIL 2016

CERTIFICATE

This is to certify that this Dissertation entitled "**THE STUDY OF THE EXPRESSION OF MUC1 IN GASTRIC CARCINOMAS AND ITS CORRELATION WITH THE CLINICO - PATHOLOGICAL VARIABLES**" is the bonafide original work of **Dr.A.ANITHA CHELLAM**, in partial fulfillment of the requirement for M.D., (Branch III) in Pathology examination of the Tamil Nadu Dr. M. G.R Medical University to be held in April 2016.

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DECLARATION

I, **Dr. A.ANITHA CHELLAM**, solemnly declare that the dissertation titled "**THE STUDY OF THE EXPRESSION OF MUC1 IN GASTRIC CARCINOMAS AND ITS CORRELATION WITH THE CLINICO-PATHOLOGICAL VARIABLES**" is the Bonafide work done by me at the Institute of Pathology, Madras Medical College under the expert guidance and supervision of **Prof**. **Dr. V. RAMAMOORTHY M.D.**, Institute of Pathology, Madras Medical College. The dissertation is submitted to the Tamil Nadu Dr. M.G.R Medical University towards partial fulfillment of requirement for the award of M.D., Degree (Branch III) in Pathology.

Place: Chennai

Date: **Dr.A.ANITHA CHELLAM**

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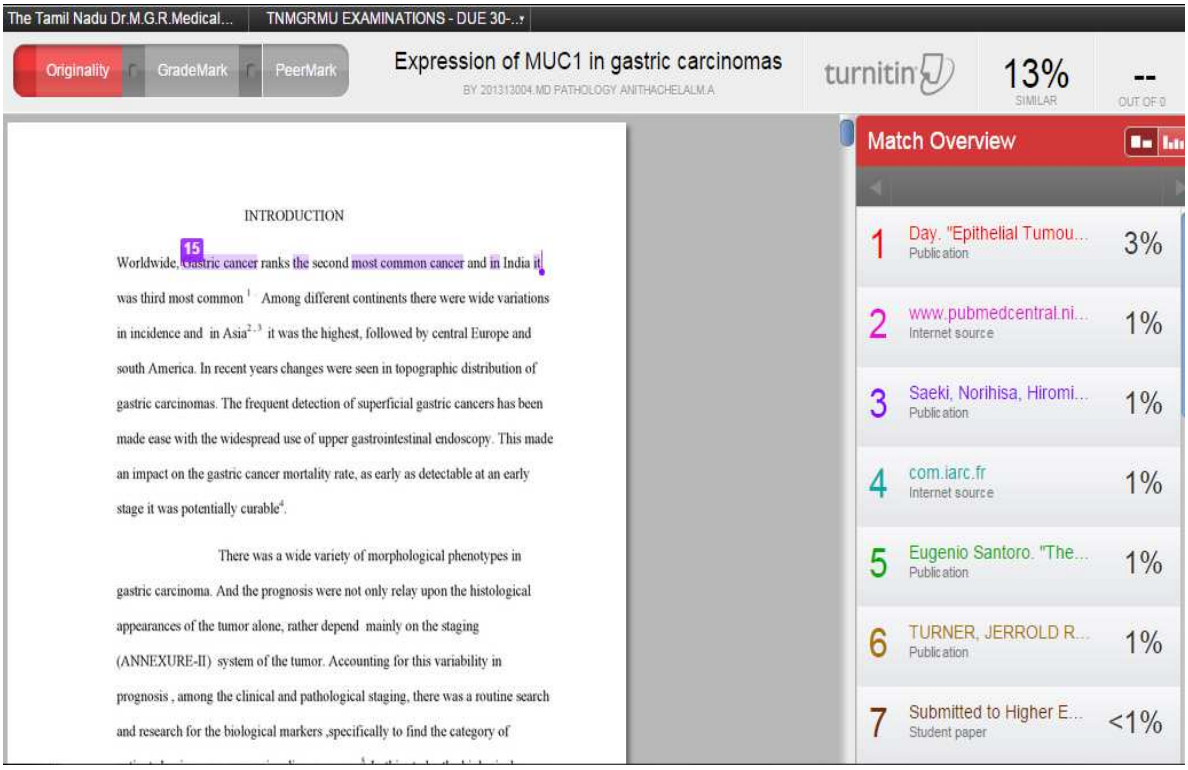
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Expression of MUC1 in gastric carcinomas
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INTRODUCTION
Worldwide, gastric cancer ranks the second most common cancer and in India it was third most common [1] Among different continents there were wide variations in incidence and in Asia[2-3] it was the highest, followed by central Europe and south America. In recent years changes were seen in topographic distribution of gastric carcinomas. The frequent detection of superficial gastric cancers has been made ease with the widespread use of upper gastrointestinal endoscopy. This made an impact on the gastric cancer mortality rate, as early as detectable at an early stage it was potentially curable[4].
There was a wide variety of morphological phenotypes in gastric carcinoma. And the prognosis were not only relay upon the histological appearances of the tumor alone, rather depend mainly on the staging (ANNEXURE-II) system of the tumor. Accounting for this variability in prognosis , among the clinical and pathological staging, there was a routine search and research for the biological markers ,specifically to find the category of
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CERTIFICATE OF APPROVAL

To
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Dear Dr.A.Anitha Chellam,

The Institutional Ethics Committee has considered your request and approved your study titled **"The study of expression of the MUC-1 in gastric carcinomas and its correlation with the clinicopathological variables". No.10102014.**

The following members of Ethics Committee were present in the meeting held on 07.10.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr.C.Rajendran, M.D.,	: Chairperson
2.	Dr.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
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4.	Prof.R.Nandhini, M.D., Inst.of Pharmacology, MMC	: Member
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10.	Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

31/10/14

Member Secretary, Ethics Committee

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ABBREVIATIONS

G I	:	Gastro - Intestinal
WHO	:	World Health Organization
MUC1	:	Mucin-1
HNPCC	:	Hereditary Non – Polyposis Colorectal Cancer
OGJ	:	Oesophago – Gastric Junction
EGC	:	Early Gastric Carcinoma
AGC	:	Advanced Gastric Carcinoma
IHC	:	Immuno histochemistry
GIST	:	Gastro – Intestinal Stromal Tumour
HRP	:	Horse – Radish Peroxide
AJCC	:	American Joint Committee on Cancer
IT	:	Intestinal type
DT	:	Diffuse type
LVI	:	Lymphovascular invasion
PNI	:	Perineural invasion

CONTENTS

ABSTRACT

INTRODUCTION

Worldwide, Gastric cancer is the second most common type of cancer. Of the gastric cancer, adenocarcinoma is the most common malignancy. It comprises over 90% of all gastric cancers. Gastric mucins are synthesized by gastric epithelial cells which are cytoprotective. Mucins are glycoprotein with high molecular weight, which are membrane bound or secreted products synthesized by secretory epithelial cells. Mucins in general are classified as neutral and acidic. Normal gastric mucin is of neutral type. In neoplastic transformation of gastric mucosa, the neutral mucin production is decreased.. More than 15 mucin genes have been identified. MUC-1 expressed in tumor may function as an anti-adhesion molecule that inhibits cell to cell adhesion, inducing the release of cells from the tumor. In these manners MUC-1 expression may be associated with invasive or metastatic properties of tumor cells, resulting in poor prognosis for patients with gastric carcinoma showing MUC-1 expression.

AIM

To study the expression of MUC1 in gastric carcinomas and its correlation with the clinico pathological variables.

MATERIALS AND METHODS

From the period June 2013-2015 ,of the 126 gastrectomy specimens received, 50 cases of gastrectomy specimens were subjected to immunohistochemistry marker, MUC1 and analysed with various clinicopathological parameters including age, sex, site, gross type, histological type, grading, TNM staging, lymphocytic infiltration, lymphovascular invasion, perineural invasion and its correlation with MUC1 Mucin, expression and the results were tabulated and statistically evaluated .

RESULTS

In the study period of 2 years from June 2013-June 2015, Gastric cancer had a peak incidence in the age group of 51 – 60 years, with the mean age of 55.5 years with 70% - in males and 30% in females. Males predominate in the ratio of **2 .3 : 1** . On immunohistochemistry with MUC1,the expression was membranous / cytoplasmic positivity (graded as 1+, 2+, 3+, Negative) which was seen in 64% of cases. An increase in expression of MUC1 positivity was seen with increasing age and intestinal type of gastric adenocarcinomas.

KEY WORDS

Gastric Adenocarcinoma, anti-adhesion, MUC1 expression, cytoplasmic.

INTRODUCTION

Worldwide, Gastric cancer ranks the second most common cancer and in India it is third most common[1]. Among different continents there were wide variations in incidence and in Asia[2, 3] incidence was the highest, followed by central Europe and South America. In recent years changes were seen in topographic distribution of gastric carcinomas. The frequent detection of superficial gastric cancers has been made easy with the widespread use of upper gastrointestinal endoscopy. This made an impact on the gastric cancer mortality rate, as carcinomas detectable at an early stage were potentially curable[4].

There was a wide variety of morphological phenotypes in gastric carcinoma. The prognosis not only rely on the histological appearances of the tumor alone, but rather depend mainly on the staging (ANNEXURE-II) system of the tumor. Accounting for this variability in prognosis, among the clinical and pathological staging, there was a routine search for the biological markers, specifically to find the category of patients having aggressive disease course[5] .In this study, the biological behaviour of gastric cancer has been studied using the immuno histochemical expression of protein MUC-1 Mucin.

MUC-1, Mucin is a trans membrane glycoprotein with an extracellular domain consisting of a variable number of highly conserved tandem repeats of 20 aminoacids, a trans membrane domain and a cytoplasmic tail of 69 aminoacids[6,7,8,9,10].

MUC-1 expressed in tumor may function as an anti-adhesion molecule that inhibits cell to cell adhesion, inducing the release of cells from the tumor[11,12]. In this manner MUC-1 expression may be associated with invasive or metastatic properties of tumor cells, resulting in poor prognosis for patients with gastric carcinoma showing MUC-1 expression.

Carcinoma associated with MUC-1 and synthetic tandem repeats of MUC-1 mucin core peptide, suppress human T cell proliferative response and the high levels of MUC-1 mucin are correlated with immunosuppression in adenocarcinoma patients and this immunosuppression by MUC-1 result in poor prognosis of gastric carcinoma patients[13].

Hence the patients expressing MUC-1 mucin have poorer prognosis and aggressive tumor behavior. Thus the routine evaluation of mucin MUC-1 could be useful in identifying patients with aggressive disease and contribute to a better therapeutic approach .

In this study of 50 cases, an attempt is made to study the expression of MUC-1 immunohistochemically and to compare it with the parameters clinicopathologically.

AIMS AND OBJECTIVES

1) To identify the incidence and distribution of gastric carcinoma in patients admitted in Government General Hospital, Chennai from June 2013 to June 2015.

2) To study the histomorphological features of gastric carcinoma including tumor size, tumor location, macroscopic appearance, histological type, grade, depth of infiltration, lymph node status, stage ,presence of lympho-vascular invasion, perineural invasion, lymphocytic response.

3) To study the immunohistochemical expression of MUC-1 in gastric carcinoma.

4) To determine the correlation of MUC-1 expression with known prognostic factors such as tumor size, histological type, grade, depth of infiltration, lymph node status, stage, presence of lymphocytic infiltration, lympho-vascular invasion and perineural invasion.

REVIEW OF LITERATURE

ANATOMY[14]

Stomach is a variable sized distensable bag located a few centimeter below the diaphragm. It is divided into 5 regions .An ill defined area connects the G.E junction is the cardia. The portion of stomach below cardia is the fundus .The main portion which lies below the fundus is the body or corpus. The distal portion is the antrum , separated approximately at the incisura anguaris from the body. The distal most is the narrow channel (1-2cm) the pylorus, which follows the antrum ,connects stomach with the duodenum.

HISTOLOGY[14]

In view of its epithelial components ,stomach is a complex organ. Mucosa of stomach is fundic and antral type.

Fundic type mucosa is seen in fundus and body. It consists of fundic or oxyntic glands, which constitutes approximately 80% of the mucosal thickness. The superficial cells (20%) consists of tall columnar foveolar cells which produce neutral mucin .The fundic glands are composed of parietal cells secreting acid and Zymogen (chief)cells secreting pepsin. Antral type mucosa is seen in the antrum, pylorus and cardia, where the loosely packed deeper glands secrete mucin. In antral type mucosa the ratio of mucinous glands to overlying foveolae is roughly 1:1.

The lamina propria is composed of inflammatory cells comprising of only a minimal number of lymphocytes, eosinophils , plasma cells and mast cells.

The sub mucosa is composed of loose connective tissue containing numerous elastic fibers , arteries ,veins , meissner's nerve plexus and lymph vessels.

The muscularis propria consists of inner circular and outer longitudinal layer and the outer most layer is the serosa .

GASTRIC CARCINOMA

INTRODUCTION

Gastric carcinoma are malignant tumors of stomach arising from gastric glandular epithelium. In 1600 BC, the first case of gastric cancer was reported in Ebers papyrus and in the second century AD in the Hippocrates reports related by Galen in Rome[15] .A possible description of a gastric cancer could be read in Avicenna's medical encyclopedia ,at the end of the first millennium AD. Despite this in the 18th century, gastric cancers were largely unknown because benign and malignant gastric ulcers were only described later by J.Cruveilhier, in 1835.

The official history of gastric cancer surgery began 40 years later,when Jules Emile Pean, a very famous French surgeon , performed the first gastric resection for cancer in 1879[16],during which the official history of gastric cancer

surgery began. In 1881,In veinna the first successful subtotal resection with gastro duodenal anastamosis was performed by Theodor Billroth[17].

CLASSIFICATION

The most common malignancy of stomach is the adeno carcinoma, accounting to 90% of all gastric cancers .Several systems of classification were proposed later. Lauren classification was one of the earliest proposed in 1965,enumerates 2 types of gastric carcinoma -Intestinal and Diffuse type[18].Followed by Ming in 1977,divided adeno carcinoma into 2 types based on growth pattern 1) Expanding and 2) Infiltrative. And In 1977 WHO classification **(ANNEXURE-III)** was proposed based on histomorphology.

EPIDEMIOLOGY

Incidence of gastric carcinoma varies with geography. It is up to 20 fold higher in Japan, Coast Rica, Chile, Eastern Europe when compared to Northern Europe, North America, South East Asia and Africa. In high incidence region like Japan,35% of newly detected cases were of early gastric cancer (i.e) tumor limited to mucosa and sub mucosa. This is because of mass endoscopic screening programs[14].Japan and Korea have the highest gastric cancer rate in the world[19]. Based on the study of National cancer Registry program of India in 2001,the number of new Gastric cancer were approximately 35,675 (n-23,785 in Males,11890 in Females)[20].

Southern part of India has four times higher incidence rates of gastric cancer when compared to Northern parts. In southern part of India, among the

six registries, Gender wise higher incidence rate was reported from Chennai for both the genders and the age standardized incidence rates are 13.6/100,000 in Males and 6.5/100,000 in Females[20].On Comparing Five year survival rates ,it was higher up to 95% in early gastric cancers, whereas 10 to 20% in advanced gastric cancers [21].

AGE AND SEX

Gastric carcinomas are very rare in less than 40 years of age. It is more common in older age group in both the sexes. In Males, intestinal type is more common, whereas in Females and younger individuals diffuse type is the most common type [22].

ETIOLOGY

HIGH RISK FACTORS

Low socio economic status, salt intake, smoked meat or fish, pickled vegetables, soya beans , peppers, and Host factors, Helicobacter pylori have high risk for developing gastric carcinoma.

DIET

The diets mentioned above have low level of micronutrients, antioxidants, vitamins, and these favors the intraluminal formation of genotoxic agents such as N- nitrosocompounds that lead to the development of gastric carcinoma.

H.pylori

Long standing H. pylori infection results in chronic gastritis, atrophic gastritis and intestinal metaplasia which result in increased risk of intestinal type of gastric carcinoma.

In people having Blood Group A, and in those having family history of gastric cancer or pernicious anemia there is high incidence of gastric adenocarcinoma ,Diffuse type.

LOWEST RISK

Individuals with consumption of fresh fruits, vitaminC rich foods, vegetables, carotenoids, folates, tocopherols are found to have lowest risk of developing gastric cancer.

PATHOGENESIS

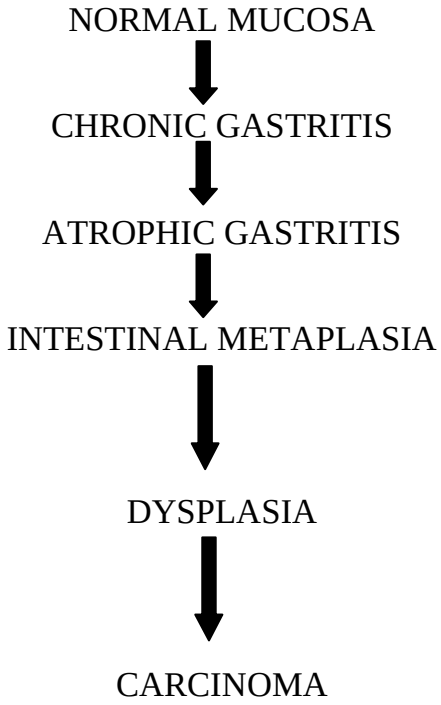
Germline mutation in CDH1 encodes E-cadherin protein that contributes to epithelial intercellular adhesion. It is usually associated with familial gastric cancer, mainly of diffuse type. CDH1 mutations are also seen in about 50% of sporadic cases of diffuse type gastric carcinomas. Also individuals with BRCA2 mutations are at increased risk of developing gastric cancer diffuse type[23].

Mutation of beta catenin, a protein that binds to both E-cadherin and APC is seen in intestinal type of gastric cancer[23].Microsatellite instability and hypermethylation of several genes including BAX, TGFbetaRII, IGFRII and

INK 4a/P16 also contribute to gastric cancer intestinal type. P53 mutation is present in majority of sporadic gastric cancer of both types. [23]

Patients having mutations of DNA mismatch repair genes and with HNPCC have increased frequency of gastric cancer[24].Patients with Peutz - jegher's syndrome also show an increased risk of gastric cancers[25].

Gastric carcinogenesis[26] is a multistep and multi factorial process that involve progression from



LOCALIZATION / TOPOGRAPHY OF GASTRIC CARCINOMA

Distal stomach in antro pyloric region and along the lesser curvature is the most common site of gastric cancer. Recently cardiac region of stomach is found to have more incidence. Carcinomas of corpus may be located either on the Greater or Lesser curvature.

Early Gastric cancers are more commonly seen along the lesser curvature in the middle part of stomach, whereas Advanced gastric cancers are more common in antral region followed by corpus region.

EARLY GASTRIC CANCER (EGC)

This is limited to the mucosa or sub mucosa only, irrespective of lymphnode status. After histological examination EGC is subdivided into two group. Intra mucosal and Sub mucosal carcinoma. The presentation is somewhat at lower age [27] and generally the duration of symptoms are longer[28]. Early gastric cancer are otherwise called as surface carcinoma[29], superficial spreading carcinoma[30] and Cancer gatrique au de'but[30].The term early gastric cancer denotes that the gastric cancer is potentially curable and does not denote the genesis of the cancer[32].In countries like Japan, it is due to the routine and regular screening programs ,that the increasing numbers of early gastric cancers are being detected.

ADVANCED GASTRIC CANCER (AGC)

By definition this type of cancer has spread beyond the sub mucosa into muscularis propria and beyond,irrespective of lymphnode status. The term advanced indicate that treatment of this tumor is very difficult and they have decreased survival and it does not denote the higher stage of the disease.

PRE CANCEROUS CONDITIONS

1) Epithelial polyp
2) Chronic atrophic gastritis –More common condition leading to carcinoma
3) Chronic ulcer
4) Intestinal metaplasia
5) Gastric remnants
6) Hyperplastic Gastropathy

CLASSIFICATION OF INTESTINAL METAPLASIA

Based on their cell type and functional features it is divided into 2 types 1) Complete and 2) Incomplete

Complete Intestinal Metaplasia

Gastric mucosa assumes the appearance of small intestine without villi. Glands are lined by absorptive cells,goblet cells, paneth cells, endocrine cells. Mucin can be sulphomucin ,sialomucin or both.

Incomplete Intestinal Metaplasia

Instead of absorptive cells, columnar cells between the goblet cells resemble foveolar mucus cells. Mucin can be neutral, sulphomucin or sialomucin.

RECENT CLASSIFICATION OF INTESTINAL METAPLASIA[22]

TYPE I-Complete intestinal metaplasia

TYPEII-Incomplete intestinal metaplasia

TYPE III-Incomplete intestinal metaplasia with predominant sulphated mucin.

MACROSCOPIC APPEARANCE OF GASTRIC CANCER

Japanese Gastroenterological endoscopic society devised a sub classification for gross appearance of early gastric cancer based on macroscopic appearance on endoscopy and in gastrectomy specimens. They were divided into 3 main types and 3 subtypes

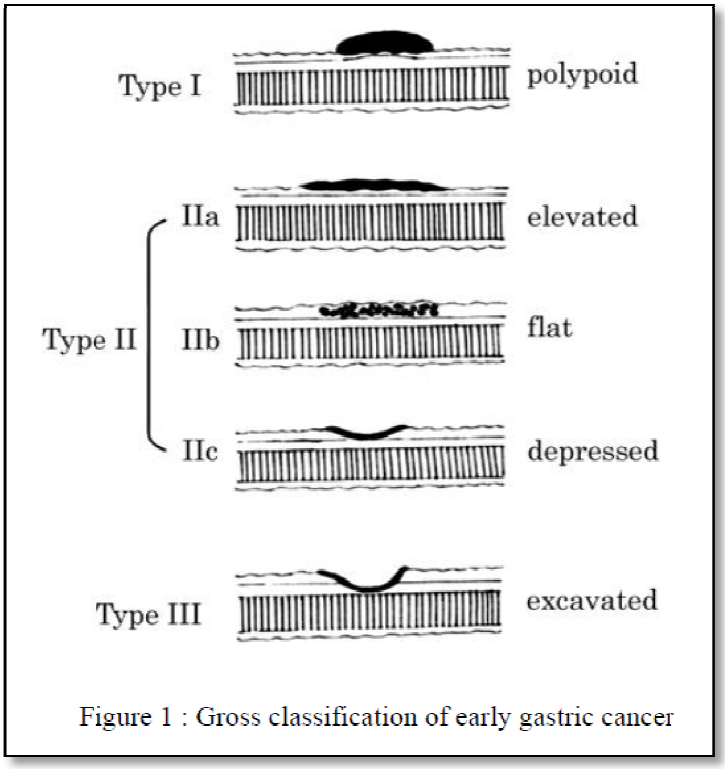


Figure 1 : Gross classification of early gastric cancer

TYPE I – **Protruded**-The tumor projects clearly into the lumen and includes all polypoid ,nodular and villous tumors

TYPE II – **Superficial**-This is further subdivided into 3

TYPE II a - Elevated above surrounding mucosa by few millimeter,seen as well circumscribed flat plaque.

TYPEII b - Macroscopically no visible abnormality. Flat.

TYPEII c –Depressed. Surface slightly depressed below the adjacent mucosa

TYPEIII – **Excavated**-Ulceration of variable depth into the gastric wall.

Macroscopic types of advanced gastric cancers can be understood from the scheme depicted by Dr. Bormann, who was a German Surgeon and a pathologist

TYPE I –Polypoid / Nodular

TYPEII –Ulcerative, localized/ fungating

TYPEIII –Ulcerative, infiltrative

TYPEIV –Diffusely, infiltrative

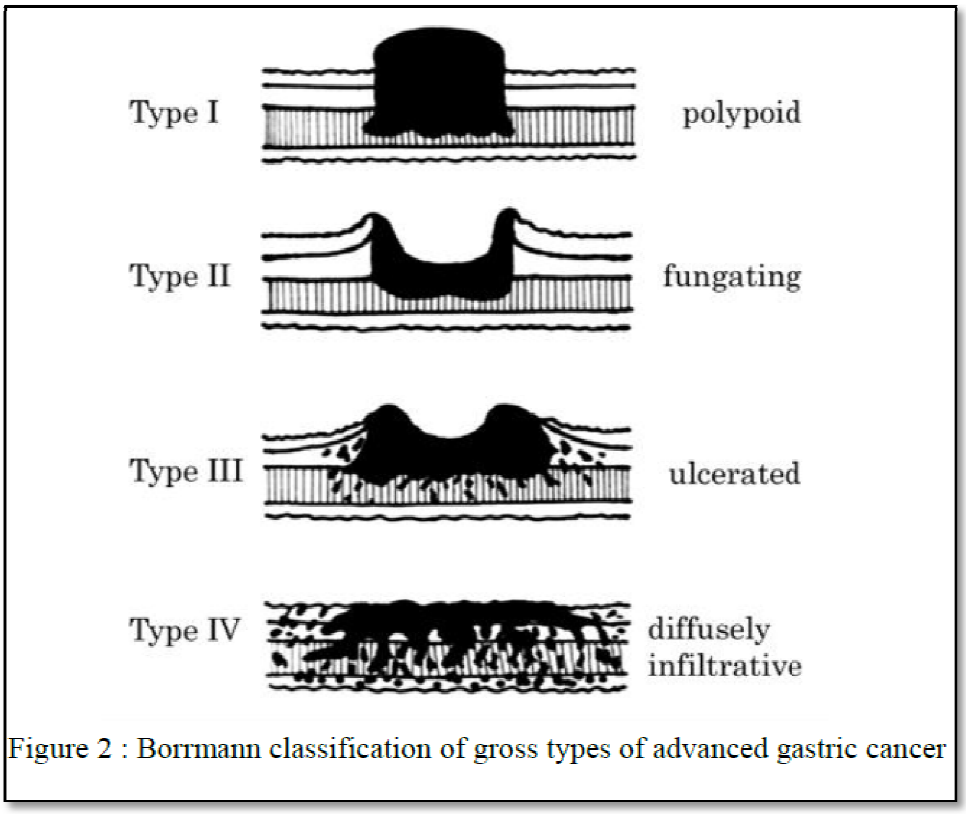


Figure 2 : Borrmann classification of gross types of advanced gastric cancer

Ulcerated tumors most commonly occur in the lesser curvature, antral region. The ulcers are large with raised rolled out edges, irregular margins and necrotic shaggy base[33].Polypoid, Nodular and fungating tumors occur in the body of stomach, greater curvature, posterior wall or fundus. Infiltrative cancers produce plaque like lesions, spread superficially in the mucosa and sub mucosa. It is accompanied by thickness of entire wall of the stomach producing the Leather bottle stomach or the so called Linitis plastica. Many Gastric carcinomas gives the gelatinous appearance secreting considerable amounts of mucin, (so called colloid carcinomas.)

Gastric adenocarcinomas are either gland forming tumors composed of tubular, papillary or acinar patterns or they are composed of complex mixture of isolated or discohesive cells[34].

Several classification systems were proposed and they include Ming, Carniero and Goseki. Despite these the most commonly used were those of WHO[35] (**ANNEXURE III**) Classification and Lauren.

WHO CLASSIFICATION

Tubular Adenocarcinoma

Tubular adenocarcinoma composed predominantly of neoplastic tubules often showing irregular branching and anastomosis embedded in or surrounded by fibrous stroma. The neoplastic cells are columnar, cuboidal or flattened with intraluminal mucin. The degree of cytological atypia varies from low to high grade. An oncocytic variant of this type and poorly differentiated variant sometimes called as solid carcinoma has been described[36].

Papillary Carcinoma

These are well differentiated carcinomas with papillary architectures which are elongated finger like processes lined by cuboidal cells with central fibrovascular core composed of connective tissue .Tubular differentiation may also been seen in this tumor referred as papillotubular. Micropapillary architecture has been seen rarely. Polypoid mass into the lumen of the stomach is the typical appearance of this tumor.

Mucinous Carcinoma

According to WHO, carcinomas containing more than 50% of extracellular mucin are called as mucinous carcinomas .In this there are two

sub types 1) The neoplastic cells form glands lined by columnar mucous secreting cells called as well differentiated type.2) In this there are disaggregated ribbons or clusters of cells which appear to be floating in the lakes of mucin referred to as poorly differentiated type. Mucin may be seen in the inter glandular stroma , scattered signet ring cells when present ,do not dominate the histological picture. They most commonly occur as polypoid , ulcerative ,or fungating masses.

Signet Cell Carcinoma

According to WHO this type of tumor is defined as carcinomas composed predominantly of single cells or small clusters of cells containing intra-cytoplasmic mucin vacuoles and accounting for more than 50% of the tumor. A classical signet ring cell appearance was due to an expanded, globoid, optically clear cytoplasm and the cells contain nuclei which push against cell membranes. These contain acid mucin and stain with Alcian blue at PH 2.5.

There are also cells with no mucin and cells with eosnophilic granular cytoplasm containing neutral mucin .This tumor is most commonly seen in younger patients and in distal stomach. The signet ring cell carcinomas tend to infiltrate the stomach wall diffusely and are accompanied by marked fibrosis giving rise to Linitis Plastica appearance in gross examination.

LAUREN'S CLASSIFICATION

Lauren[18] (1965) classified gastric adenocarcinomas histologically into two main types Intestinal and Diffuse .And those tumors having equal proportion of these two components are called as Mixed carcinomas. Carcinomas that are too undifferentiated to fit in either of these category are placed in Indeterminate category.

INTESTINAL TYPE

Intestinal type tumors have a glandular pattern usually accompanied by tubules ,papillary formations or solid components. The glands range from well differentiated to moderately differentiated grade. Sometimes poorly differentiated tumor at the advanced margins. The glandular epithelium is composed of pleomorphic cells with large hyperchromatic nuclei often with numerous mitoses. The adjacent gastric mucosa often shows chronic gastritis ,with widespread intestinal metaplasia and sometimes dysplasia. Intestinal type are commoner in the elderly and males.

DIFFUSE TYPE

These are predominantly composed of poorly cohesive diffusely infiltrating small tumor cells with indistinct cytoplasm and hyperchromatic nuclei, glandular formation may occur in the superficial part of the tumor. Signet ring cells are common and there may be extracellular mucin in the stroma. Desmoplasia is more pronounced and there may be no accompanying

metaplasia or dysplasia .Diffuse tumors usually occur at an younger age groups with equal sex incidence.

MING CLASSIFICATION

This expands Lauren's classification by adding pyloro cardiac gland carcinoma[38] a third type. These present as well demarcated fungating tumors. These tumors are commoner in men, and are characterized microscopically by varying sized glands showing tubular or papillary pattern .Cells that often show striking vacuolation or clear cell change and stain brilliantly with periodic acid Schiff reaction.

GOSEKI CLASSIFICATION

This classification of gastric cancers by Goseki based on the degree of differentiation into tubules and the amount of mucin present intracellularly[39] and divided into four histological types.

GROUP I- Well differentiated tubules with poor intracellular Mucin

GROUPII- consists of well differentiated tubules with plentiful intracellular mucin

GROUPIII – consists of poorly differentiated tubules and poor intracellular mucin

GROUP IV- consists of poorly differentiated tubules and plentiful of

intracellular mucin

CARNEIRO CLASSIFICATION

This classification by Carneiro et al is a much simpler one in which the division comes as glandular,solid,isolated cell carcinomas and a mixed type which have a mixture of both glandular and isolated cells[34].

RARE VARIANTS

Adenosquamous carcinoma[40]

Squamous cell carcinoma[41]

Hepatoid adenocarcinoma[42]

Choriocarcinoma[43]

Medullary carcinoma with lymphoid stroma[44]

Small cell carcinoma[45]

Parietal cell carcinoma[46]

Gastric carcinoma with rhabdoid differentiation[47]

Carcinosarcoma[48]

SPREADING OF GASTRIC CARCINOMA

Spreading of gastric cancer is particularly common with diffuse carcinomas and signet ring cell type carcinomas, in which spreading occur directly by penetrating the serosa and organ infiltration like liver, spleen,

pancreas, transverse colon and omentum. The depth of invasion of wall of the stomach directly correlates with the incidence of lymphatic spread. The lymphnodes which are commonly involved are nodes of left gastric, common hepatic, pancreatic, splenic and celiac artery .If there is more distant spread, it involves mesenteric and para aortic nodes. The spread to left supra clavicular nodes via the thoracic duct (nodes of troisier and virchow) is not uncommon.

The spread by hematogenous route most commonly involves liver, followed by lung ,peritoneum,adrenal,skin and ovary(krukenberg tumor).The unusual sites such as kidney,spleen,uterus and meninges are involved in diffuse type of gastric carcinomas[49].

STAGING OF GASTRIC CANCER

The TNM staging system[50] (**ANNEXURE II)** is widely used in western countries. It is recommended and is the best available predictor of prognosis.

PROGNOSIS

The prognosis of gastric cancer varies according to different countries with the best results of overall 5 year survival rate of 46% for advanced and 89% for early gastric carcinomas in Japan[51].In western countries the overall survival rate is between 4% and 13%[52].According to a recent study which indicated there was 63%cumulative 5 year risk of progression into advanced cancer, from an untreated early gastric cancer[53].

PROGNOSTIC FACTORS

Any variable, which provides information, that are useful to assess the outcome of the disease at the time of diagnosis are called as prognostic factors. They are classified into clinical, morphological, genetic/molecular factors.

The clinical factors associated with poor prognosis are younger age ,large tumor size and gastric cancers at the proximal region[52].For the cardia tumors the 5 year survival rates are under 20% [54] and 7 months of median survival only[55].

The pathological factors playing a key role in prognosis assessment are as follows

1) Stage Of The Tumor

It is the most significant factor , which incorporates the depth of invasion, the deeper the penetration ,the greater the chance of metastasis. This feature directly correlates with gross appearance of the tumor, such as the large intra luminal mass have lower rates of metastasis than those growing primarily within the wall.

2) Microscopic Type And Grading Of The Tumor

Lauren's Intestinal type of tumors behave relatively better than diffuse types[56].

3) Regional Nodal Involvement

With nodal positive cases, the 5 year survival rate drops to less than 10% when compared to node negative cases with 50% survival. The involved number of nodes is a prognostically significant factor. As the number of positivity in lymph node increases, the overall survival rate decreases[57].

4) Size Of The Tumor

Though smaller size tumors are associated with better prognosis, it is linked closely with the depth of invasion /penetration[51].

5) Lymphatic Invasion

It is associated with poor prognostic indicator and strong association with nodal metastasis and poor patient survival.

6) **Vascular Invasion-**

The tumor cells infiltrate into the vascular spaces. Vascular invasion is the predictor of visceral metastasis and recurrence.

7) **Perineural Invasion**

It is the sign of poor prognosis

Other than the above mentioned factors ,poor prognostic factors include tumor necrosis, infiltrative tumor margins and surgical margin infiltration by tumor cells.

In the study done by Y.E. Joo[77] et al the mean age of gastric carcinoma was 58.7 years with a range from 28 to 79 years , an average tumor size of 5.2 cm and nodal metastasis in 51.3% cases .

In the study done by Nobuyuki Igarashi et al the incidence of gastric cancer in men and women was 74.1% and 25.9% respectively.

In the study of N.E. Tzanakis et al[74] 51.6% tumors in the antrum , an average tumor size of 5.1 cm

Daniela Lazar et al[75] in his study observed 8.2% of Bormann type I tumors, 32.7% of type II tumors, 36% of type III tumors and 14.7% of type IV tumors, observed 50.8% tumors in the antrum. and the most common histological subtype of gastric cancer is Tubular carcinoma.

The most common histological subtype of gastric cancer is Tubular carcinoma Y.Kakeji et al[78]. The most common histological subtype (Lauren's) based on the observations of the study made by Casasola et [a80] was the intestinal type.

A higher proportion of T3 tumors, closely followed by T2 tumors were observed in the study of Giovanni de Manzoni et al[81], and Y.E. Joo et al[77].

the study by Czyzewska J et al [79] nodal metastasis was observed in 55.6% of cases.

Many molecular biomarkers, play a significant role in gastric carcinoma management.40 to 50% of gastric carcinoma show DNA Aneuploidy and they have significant association with both distant metastasis and lymphnode metastasis. Aneuploid tumors have lower survival rate than diploid

tumors[58].HER2neu/c erb2,a trans membrane epidermal growth factor receptor protein, over expression are known to be associated with poorer outcome[59].Germline mutations of E-cadherin gene (CDH-1),which plays a role in maintenance of intercellular connections are associated with highly aggressive diffuse type gastric cancers[60].Increased cathepsin D expression ,increased proliferation indices and loss of F hit protein are associated with decreased survival.MUC-1,Mucin a trans membrane glycoprotein, expressed in tumors may function as anti-adhesion molecule, that inhibits cell to cell adhesion inducing release of tumor cells[11,12].In these manners,MUC-1 expression may be associated with invasive or metastatic properties of tumor cells, resulting in poor prognosis for patients with gastric carcinomas.

MUCIN PROFILE IN STOMACH

Gastric mucins are synthesized by gastric epithelial cells which are cytoprotective. Mucins are glycoprotein with high molecular weight ,which are membrane bound or secreted products synthesized by secretory epithelial cells[61].

A tandem repeat region rich in threonine /serine are characteristic of mucins which are O- glycosylation sites. The difference in tandem repeat sequence length and non repetitiveness makes each mucin an unique and distinct entity[62].

Mucins in general are classified as neutral and acid mucin of these, Acid mucins are of two types

1) Sulphated /sulphomucin and

2) Carboxylated/sialomucins

Normal gastric mucin is of neutral type .Small amount of acid mucins such as sialomucin, sulphomucin are produced in foveola, neck cells of the fundus, foveola of antrum and cardiac glands of stomach[62,63].

In neoplastic transformation of gastric mucosa, the neutral mucin production is decreased. In intestinal metaplasia, a common precursor condition of carcinoma stomach[62], the transition to acid mucin from neutral mucin occurs. These acid mucin produced during transition stage and gastric adenocarcinoma are predominantly of sulpho mucin type.

Sulphomucin an acid mucin, characteristic of mature surface mucin cells are predominantly seen in well differentiated adenocarcinoma. The sialomucin, also an acid mucin, characteristic of intestinal goblet cells [64] are seen predominantly in moderately differentiated and poorly differentiated adenocarcinoma.

The mucin secreted in mucinous adenocarcinoma are O acylated form of sialomucin, acidic mucin. This variant has good prognosis than the Signet ring cell carcinoma stomach.

By special stain studies acid mucin and neutral mucin are clearly identified, such as PAS-periodic acid Schiff, combined Alcian blue Ph 2.5 PAS.

MUCIN GENE EXPRESSION IN NORMAL GASTRIC MUCOSA AND GASTRIC ADENOCARCINOMA

Human gastric epithelium has an unique mucin gene pattern which becomes altered markedly in pre neoplastic and neoplastic conditions. More than 15 mucin genes have been identified and they are categorized into

1) **Membrane Associated Mucin**

MUC1,3,4,12,13,15,16,17,20

2) **Gel Forming Mucin**

MUC2,5AC,5B,6

3) **Soluble Form**

MUC7

In normal stomach MUC1,MUC5AC increased expression is seen in surface epithelium. MUC6 seen in deep gastric glands.

MUC-1

Expressed in apex of the cell .It has inhibitory role in cell to cell adhesion, cell to stromal interaction and cytotoxic immunity. By interacting

with EGFR it functions as a signal transducer and participates in carcinogenesis.

It is the marker for aggrssiveness.MUC-1 is also called as polymorphic epithelial mucin (PEM).

MUC-1 belongs to the mucin family (MUC-1 to MUC21), MUC-1 protein on cell surface consists of N- and C- terminal submits designated as MUC1-N and MUC1-C respectively [66,67].

MUC-1 FUNCTION IN GASTRIC CARCINOGENESIS[66, 67]

Contrary to its protective function in normal gastric epithelial cells, the gene is silenced in intestinal metaplasia, a pre-neoplastic lesion. Indeed MUC-1 has been considered as an oncoprotein, because there is accumulating evidence which suggests its cancer promoting function.

Moreover MUC1 could have some role in gastric carcinoma stem cells, as it acts as a growth factor receptor on undifferentiated human embryonic stem cells and is expressed in AML stem cells. Intriguingly, it is also known that MUC1 facilitates cancer cell survival under hypoxic and nutrient deprived conditions by regulating glucose and lipid metabolism and the cellular energy state.

RELATIONSHIP BETWEEN MUCIN AND PROGNOSTIC INDICATORS[6]

To obtain a more precise relation between mucin and prognostic indicators, a semi quantitative analysis was performed for mucin expressing cells in the total tumor bearing population. We reviewed five to ten fields of each cancerous tissue at high magnification and counted the number of cells expressing diffuse and membranous type. The analysis graded as +++ if 50% to 100% cancer cells stained positive for mucins, if ++ if 10 % to 50% cancer cells stained positive and + if less than 10% of cancer cells were stained positive for mucin staining.

- **+++ - if 50% to 100% of cancer cells stained positive**
- **++ - if 10 % to 50% of cancer cells stained positive**

and

- **+ - if less than 10% of cancer cells stained positive**

for mucin MUC-1 staining

Wang Zg et al [84](2012) studied 292 gastric cancer cases and found no significant association between MUC1 expression with age, gender, depth of invasion, lymph node metastasis and Lauren classification

Reis, et al[87] (2014) studied 55 cases of gastric carcinoma and found significant association between MUC1 expression with lymphatic invasion and, nodal metastasis and no significant results with advanced stage.

Utsunomiya, et al[88] (2014) studied 139 cases of gastric carcinoma and found significant association between MUC1 expression with lymphatic invasion, and no significant results with nodal metastasis and advanced stage of the tumor.

Kocer, et al[89] (2014) studied 35 cases of gastric carcinoma and found significant results with MUC1 expression and Lauren's histological classification of gastric carcinoma.

IMMUNOHISTOCHEMISTRY

In 1941, Albert coons et al was the first to label antibodies directly with fluorescent isocyanate. In 1960, Nakanae and Pierce et al, introduced indirect labeling technique, in which unlabelled antibody is followed by second antibody or substrate. Various stages of development of immunohistochemistry include Peroxidase- Antiperoxidase method (1970), Alkaline phosphatase labeling (1971), Avidin Biotin method (1977) and the two layer dextrin polymer technique (1993)[69].

ANTIGEN RETRIEVAL

It can be done by the following different techniques to unmask the antigenic determinants of fixed tissue sections

1) Proteolytic enzyme digestion

2) Microwave Antigen retrieval

3) Pressure cookware antigen retrieval

4)Microwave and trypsin antigen retrieval

1) Proteolytic Enzyme Digestion

In 1976, Huank et al introduced this technique to breakdown formalin cross linkages and to unmask the antigen determinants. Trypsin and proteinase[70] were the most common used enzymes. Overdigestion, under digestion and antigen destruction are the disadvantages.

2) Microwave Antigen Retrieval

This is the most common used new technique in current practice. Micro oven heating involves boiling formalin fixed paraffin sections in various buffers for rapid and uniform heating .Antibodies against MUC1 work well after heat pretreatment in this method[69].

3) Pressure Cookware Antigen Retrieval

In 1995, Miller et al compared and proved that pressure cooking method has fewer inconsistencies ,less time consuming and can be used to retrieve large numbers of slides than in microwave method[71].

PITFALLS OF HEAT PRETREATMENT

Drying of sections at any stage after heat pretreatment destroys antigenicity. Nuclear details are damaged in poorly fixed tissues, while heating fibers and fatty tissue tend to detach from the slides. Not all antigens are retrieved by heat pretreatment. Also some antigens may show altered staging pattern.

DETECTION SYSTEMS

After addition of specific antibodies to antigens, next step is to visualize the reaction complex of antigen antibody. The methods employed here are the direct and indirect.

In the Direct method, primary antibody is directly conjugated with the label. Most commonly used labels are flourochrome, horse radish peroxidase (HRP) and alkaline phosphatase.

And the indirect method is a two step method in which labeled secondary antibody reacts with primary antibody bound to specific antigen. The use of peroxidase enzyme complex or avidin biotin complex further increases the sensitivity of immunohistochemistry stains[69].In 1993, Pluzek et al, introduced enhanced polymer one step staining ,in which large number of primary antibody and peroxidase enzymes are attached to dextran polymer backbone. This is the rapid and sensitive method[72].

Dextran polymer conjugate ,two step visualization system is based on dextran technology in Epos system. This method has greater sensitivity and is less time consuming.

MATERIALS AND METHODS

This study is both retrospective and prospective descriptive study of gastric adeno carcinomas conducted in the Institute of pathology,Madras medical college and Rajiv Gandhi Government General Hospital ,Chennai during the period from June 2013 to June 2015.

SOURCE OF DATA

The gastric adenocarcinoma cases reported in gastrectomy specimens received in Institute of pathology, Madras Medical College,from the period of June 2013 to June 2015,from the Department of Surgery ,Department of Surgical Gastro Enterology, Government General hospital .

INCLUSION CRITERIA

All the gastric carcinoma cases reported in gastrectomy specimens irrespective of age, sex are included for the study.

EXCLUSION CRITERIA

- Non- neoplastic lesions and benign tumors of stomach
- Gastric carcinomas reported in endoscopic biopsies
- Gastrectomies performed for reasons other than carcinomas

METHOD OF DATA COLLECTION

Detailed history of the cases regarding age, sex, history, type of procedure, history of neo adjuvant therapy, details of gross characteristics and nodal status were obtained for the gastrectomy cases reported during the period of study from Surgical pathology records. Hematoxylin and Eosin stained 4 μ thick sections of the paraffin tissue blocks of gastrectomy specimens were reviewed. The following clinical and pathological parameters were evaluated: Age, gender, tumor size, tumor location (Eso -cardiac, body, antrum, pangastric), macroscopic appearance (Bormann Type I, Type II, Type III and Type IV). Carcinomas were classified as Intestinal and Diffuse based on the Lauren classification and into different histological types (tubular, papillary, mucinous, signet ring cell and diffuse). Regarding the depth of invasion, the carcinomas were classified into 4 groups: T1 (invasion of mucosa and submucosa), T2 (invasion of muscularis propria and subserosa), T3 (invasion of serosa) and T4 (invasion of adjacent organs), and according to grade the carcinomas were divided into 3 groups: G1 (well differentiated), G2 (moderately differentiated) and G3 (poorly differentiated) according to the recommendations of the American Joint Committee on Cancer (2002). Lymph node metastasis was assessed and the patients were divided into 3 groups: N0 (No lymph node metastasis), N1 (metastasis in 1-6 nodes) and N2 (metastasis in 7 – 15 nodes). Carcinoma staging was done according to the standards of the American Joint Committee on Cancer (2002) and TNM classification of gastric carcinomas (**Annexure –III**). The tumors were further evaluated for the

presence of lymphocytic infiltration, perineural invasion and lympho-vascular invasion by tumor and were graded as present or absent. 50 cases of gastric adenocarcinomas of varying grades were randomly selected from the total cases and their representative formalin fixed paraffin embedded tissue samples were subjected to immunohistochemistry for marker MUC1,mucin.

IMMUNOHISTOCHEMICAL EVALUATION

Immuohistochemical analysis of marker MUC1,mucin was done in paraffin embedded tissue samples using Super-sensitive polymer HRP system based on non-biotin polymeric technology. 4 μ thick sections from formalin fixed paraffin embedded tissue samples were transferred onto gelatin coated slides. Heat induced antigen retrieval was done. The antigen was bound with mouse monoclonal antibody (Biogenex) against MUC1, protein and then detected by the addition of secondary antibody conjugated with horse radish peroxidase-polymer and diaminobenzidine substrate. The step by step procedure of Immunohistochemistry is given in (**Annexure IV)**.

Antigen	**Vendor**	**Species(clone)**	**Dilution**	**Positive control**
MUC1	BIOGENEX	Mouse	Ready to use	Colon

INTERPRETATION & SCORING SYSTEM:

The immunohistochemically stained slides were analyzed for the presence of reaction, cellular localization, percentage of cells stained and

intensity of reaction. Cytoplasmic / membrane staining was assessed for MUC1. To obtain a more precise relation between mucin and prognostic indicators, a semi quantitative analysis was performed of mucin expressing cells ,reviewed five to 10 fields at high power magnification and the analysis was graded as

- **+++ if 50–100% of cancer cells stained positive for mucins ,**
- **++ if 10–50% cancer cells stained positive,**

and

- **+if less than 10% of cancer cells were positive for mucin staining**

then the results were categorised into group 1(+), group 2 (++), or group 3 (+++).

STATISTICAL ANALYSIS

The statistical analysis was performed using statistical package for social science software version 11.5 which consisted computing the frequency counts and percentages for qualitative variables and mean for the quantitative variables. The expression of MUC1 was correlated with clinic pathological factors like age, gender, tumor site, tumor configuration, size, Lauren's type, histological types, histological grade, depth of infiltration, lymph node status, stage, lymphovascular invasion, perineural invasion, and lymphocytic infiltration using the Pearson's Chi –Square test. The expression of MUC1 were also correlated with each other using the Mc Nemar's test. T – test was used to detect the association between the mean MUC1 positive and negative groups.

OBSERVATION AND RESULTS

In the study period from June 2013 to June 2015, a total of 126 gastrectomy specimens were received in the Institute of Pathology, Madras Medical College for histological examination, of these 126 gastrectomy specimens , 124 were malignant, 2 were benign ulcers. In this total of 126 gastrectomy specimens ,124 were reported as malignant tumors ,they were 120- gastric adeno carcinoma, 2-GIST, 2 NHL and 2 were done to treat bleeding benign ulcers.

AGE AND SEX WISE DISTRIBUTION IN GASTRIC CARCINOMA

Gastric cancers had a peak incidence in the age group of 51-60 years. In the current study, the youngest age of presentation of gastric cancer is 23 years and the maximum age is 84 and mean of 55 years. And the standard deviation is 12.5 (TABLE 1 ,CHART 1).

Among the 120 cases, 83 (69.2%) cases were reported in males and 37 (30.2%) cases were reported in females (TABLE 2 AND CHART 2)

Table 1-Age Wise Distribution Of Gastric Carcinoma

Descriptive statistics					
	N	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
Age	**120**	**23.00**	**84.00**	**55.55**	**12.54628**

Age(years)	Number of cases	Percentage (%)
21-30	5	4.2
31-40	12	10.0
41-50	22	18.3
51-60	38	31.7
61-70	32	26.7
Above 70	11	9.2
Total	120	100%

Table 2- Gender Wise Distribution In Gastric Carcinoma

Gender	Number of cases	Percentage
Male	83	69.2%
Female	37	30.8%
Total	120	100%

DISTRIBUTION OF SITE OF INVOLVEMENT OF GASTRIC CARCINOMA

Among the 120 cases, 86 (71.7%) cases involved the pyloro-antrum, 25(20.8%) involved the body, 3 (2.5%) involved the fundus , 5 (4.2%) involved the OG junction and 1 (0.8%) case was in cardia (Table 3 and Chart 3)

Table 3- Distribution Of Site Of Involvement Of Gastric Cancer

Site of gastric cancer	Number of cases	Percentage
Pyloro-antrum	86	71.7%
Body	25	20.8%
Fundus	3	2.5%
Og junction	5	4.2%
Cardia	1	0.8%
Total	120	100%

DISTRIBUTION OF GASTRIC CARCINOMA ACCORDING TO GROSS MORPHOLOGY

Based on the gross morphology, the gastric tumors were divided into 4 groups according to Bormann classification & the distribution is shown in (TABLE 4 AND CHART 4)

Table 4- Distribution Of Gastric Carcinoma According To Gross Morphology

Gross	Number of cases	Percentage
Bormann type-I	19	15.8%
Bormann type-II	36	30.0%
Bormann type-III	49	40.8%
Bormann type-IV	16	13.3%
Total	120	100%

DISTRIBUTION OF SIZE IN GASTRIC CARCINOMA

Among the study samples, 56 cases (47%) had tumor less than 5 cm in size and 64 cases (53%%) were 5cm or more in size. (Table 5 & Chart 5)

Table 5- Distribution Of Size In Gastric Carcinoma

Size(cm)	Number of cases	Percentage
>= 5.00	64	53%
< 5.00	56	47%

DISTRIBUTION OF HISTOLOGICAL SUBTYPES IN GASTRIC CARCINOMA

The distribution of histological type is shown in (Table 6 & chart 6)

Table 6-Distribution Of Histological types In Gastric Cancers

Histological types	Number of cases	Percentage
Tubular	77	64.2%
Papillary	12	10.0%
Diffuse	16	13.3%
Signet ring	8	6.7%
Mucinous	4	3.3%
Lympho epithelial carcinoma	1	0.8%
Lymphoma	1	0.8%
Squamous cell carcinoma	1	0.8%
Total	120	100%

DISTRIBUTION OF GASTRIC CANCER ACCORDING TO LAUREN'S CLASSIFICATION

120 of the gastric adenocarcinomas were grouped into 2 according to Lauren's classification out of which 93 (79.5%) belonged to Intestinal type and 24 (20.5%) belonged to Diffuse type (Table 7 and Chart 7)

Table 7- Distribution Of Gastric Carcinoma According To Lauren's Classification

Lauren's type	Number of cases	Percentage
Intestinal type	93	79.5%
Diffuse type	27	20.5%
Total	120	100%

DISTRIBUTION OF HISTOLOGICAL GRADE IN GASTRIC CARCINOMA

The gastric carcinomas were graded according to AJCC recommendation and were divided into 3 groups, out of which 16 cases (11.9%) were well differentiated (G1), 61 cases (51.7%) were moderately differentiated (G2) and cases 43 (36.4%) were in poorly differentiated (G3). (Table 8& Chart 8)

Table 8- Distribution Of Gastric Carcinoma According To Histological Grading

Grade	Number of cases	Percentage
G1	16	11.9%
G2	61	51.7%
G3	43	36.4%
Total	120	100%

DISTRIBUTION OF GASTRIC CANCER ACCORDING TO DEPTH OF INVASION

In this study, 3 case (2.5%) showed invasion up to the sub mucosa (T1), 29cases (26.8%) showed infiltration into the muscularis propria or sub serosa (T2), 78cases (64.7%) showed infiltration into the serosa and 10 cases (6.0%) showed infiltration of adjacent organs (T4) (Table 9and Chart 9).

Table 9- Distribution Of Gastric Carcinoma According To Depth Of Invasion

Depth of invasion	Number of cases	Percentage
T1	3	2.5%
T2	29	26.8%
T3	78	64.7%
T4	10	6.0%
Total	120	100%

DISTRIBUTION OF LYMPH NODE METASTASIS IN GASTRIC CANCERS

This study showed that 62 cases (51.7%) had up to 6 nodes with metastatic carcinomatous deposit (N1),11 cases (9.2%) had 7 to 15 involved nodes (N2) while 47 cases (39.25%) had no node involvement (N0).(Table10 &chart 10)

Table 10 Distribution Of Nodal Metastasis In Gastric Cancer

Lymph node status	Number of cases	Percentage
N0	47	39.2%
N1	62	51.7%
N2	11	9.2%
Total	120	100%

DISTRIBUTION OF GASTRIC CARCINOMAS ACCORDING TO STAGE

In the present study, 14 cases (10.9%) belonged to stage I, 40 cases (33.6%) belonged to stage II, 49cases (41.2%) belonged to stage III and 17 cases (14.3%) belonged to stage IV. (Table 11 and Chart 11)

Table 11 Distribution Of Gastric Carcinomas According To Stage

Stage	Number of cases	Percentage
IA	2	1.7%
IB	12	9.2%
II	40	33.6%
.IIIA	41	34.5%
IIIB	8	6.7%
IV	17	14.3%
Total	120	100%

DISTRIBUTION OF OTHER PROGNOSTIC FACTORS IN GASTRIC CARCINOMA

In this study, among the 120 cases, 51cases (42.5%) had lymphovascular invasion,12(10 %) cases had perineural infiltration, 26(21.7%) cases had lymphocytic infiltration . (Table 12& Chart 12)

Table 12 –Distribution Of Other Prognostic Factors In Gastric Carcinoma

Lympho vascular invasion		Number of cases	Percentage
	Absent	69	57.5%
	Present	51	42.5%
	Total	120	100%

Peri neural infiltration		Number of cases	Percentage
	Absent	108	90.0%
	Present	12	10.0%
	Total	120	100%

Lymphocytic infiltration		Number of cases	Percentage
	Absent	94	78.3%
	Present	26	21.7%
	Total	120	100%

RESULTS OF IMMUNOHISTOCHEMICAL STUDY IN GASTRIC CARCINOMA

Of the total 120 cases, 50 cases of varying grades and stages of gastric adeno carcinomas were selected in a random manner and subjected to immune histochemical analysis with the IHC marker MUC1.

Distribution of Age and gender

Of the 50 cases, there were 35 males (70%) and 15 females (30%). There were 16 cases (32%) below 50 years of age and 34 cases (68%) more than 50 years. (Table 13)

Table 13

		Number of cases	Percentage
Age	Less than 50	16	32.0%
	More than 50	34	68.0%
Sex	Male	35	70.0%
	Female	15	30.0%

Distribution of Location/site of involvement

The tumor was located in the pyloroantrum in 35 cases (70%), body in 11 cases (22%), fundus in 1 case(2%) and in OG junction 3 cases(6%) . (Table 14)

Table 14

		No.of cases	Percentage
Site	Pyloroantrum	35	70.0%
	Body	11	22.0%
	Fundus	1	2.0%
	OG junction	3	6.0%

Distribution of Bormann gross type

5 cases (10%) belonged to Bormann Type I, 18 cases (36%) belonged to Type II, 21 cases (42%) belonged to Type III and 6 cases (12%) belonged to type IV. (Table 15)

Table 15

BormannType	No.of cases	percentage
I	5	10.0%
II	18	36.0%
III	21	42.0%
IV	6	12.0%

Distribution of Size

The tumors ranged in size from 2 to 12 cm with an average of 5.42cm. There were 20 cases (40%) with tumor size <5 cm and 30 cases (60%) with size >5cm. (Table 16)

Table16

Size	No. of cases	percentage
<5cm	20	40.0%
>5cm	30	60.0%

Distribution of Histological types

38 cases (76%) were of the tubular type, 4 cases (8%) were of the papillary type, 6 cases (12%) were diffuse carcinomas, and 2 cases (4%) were of the mucinous type.

Table17

Histological types	**No. of cases**	**percentage**
Tubular	38	76.0%
Papillary	4	8.0%
Diffuse	6	12.0%
Mucinous	2	4.0%

Distribution of Lauren's type

45 cases (90%) belonged to Lauren's Intestinal type and 5 cases (10%) belonged to the Diffuse type. (Table 18)

Table 18

Lauren's type	No.of cases	percentage
Intestinal	45	90.0%
Diffuse	5	10.0%

Distribution of Histological grading

Among the 50 cases studied 7 (14%) cases were of G1, 25 (50%) cases were of G2 and 18 (36%) cases were of G3. (Table 19)

Table 19

Grade	No. of cases	percentage
G1	7	14.0%
G2	25	50.0%
G3	18	36.0%

Distribution of T stage.

Table 20

T stage	No. of cases	percentage
T2	8	16.0
T3	32	64.0
T4	10	20.0

8(16%) cases belonged to T2, 32 (64%) cases belonged to T3 and 10 cases (20%) belonged to T4 (Table 20)

Distribution of N stage

Nodal metastasis was present in 1-6 nodes (N1) in 23 cases (46%), 7-15 nodes (N2) in 5 cases (10%) and absent in 22 (44%) cases. (Table 21a)

Table 21a

	N stage	No. of cases	Percentage
Nodal status	N0	22	44.0%
	N1	23	46.0%
	N2	5	10.0%

Distribution of other clinicopathological parameters

Of the 50 cases, 20(40%) showed lympho vascular invasion, 8 cases (16%) showed perineural invasion, and 17 (34%) cases showed lymphocytic response. (Table 21b)

Table 21b

		No .of cases	Percentage
Lymphovascular invasion	Absent	30	60.0%
	Present	20	40.0%
Perineural invasion	Absent	42	84.0%
	Present	8	16.0%
Lymphocytic infiltration	Absent	33	66.0%
	Present	17	34.0%

Distribution of TNM staging in Gastric carcinoma

6 (12%) cases belonged to stage I, 15 (30%) cases belonged to stage II, 21 cases (42%) belonged to stage III and 8 cases (16%) belonged to stage IV.

Table 22

Stage	No. of cases	Percentage
I	6	12.0%
II	15	30.0%
III	21	42.0%
IV	8	16.0%

Distribution Of MUC1 In Gastric Carcinoma

In this study ,of the total 50 cases, 9cases (18%) expressed (3+) positive reaction for MUC1, 6 cases (12%) expressed (2+) positive reaction for MUC1 ,17 cases (34%) expressed (1+) positive reaction for MUC1 and 18 cases (36%) were negative for MUC1 (Table 23 & Chart 13)

Table 23 – Distribution Of MUC1 In Gastric Carcinoma

Marker	Grading	Number of cases	Percentage
MUC1	1+	17	34.0%
	2+	6	12.0%
	3+	9	18..0%
	Negative	18	36.0%

CORRELATION OF MUC1 WITH VARIOUS CLINICO PATHOLOGICAL FACTORS

MUC1 positivity among patients below 50 years, 3+ was noted in 37.5% of cases, 2+ in 14.3% cases, 1+ in 35.3% of cases and in patients above 50 years 62.5% of cases were 3+ , 85.7% were 2+ and 66.7% were 1+. 33.3% of cases below 50 years of age and 66.7% of cases above 50 years show negativity for MUC1 (Table 24 & Chart 14)

Table 24 Correlation Of Age With MUC1Expression

In years			**MUC1**				**Total**
			Negative	**1+**	**2+**	**3+**	
Age_ group	Less than 50	Count	6	6	1	3	16
		MUC1(%)	33.3%	35.3%	14.3%	37.5%	32.0%
	More than 50	Count	12	11	6	5	34
		MUC1(%)	66.7%	64.7%	85.7%	62.5%	68.0%
Total		Count	18	17	7	8	50
		MUC1(%)	100.0 %	100.0 %	100.0 %	100.0 %	100.0 %

Pearson Chi-Square 1.220 p>0.05 (0.748)

CORRELATION OF GENDER WITH MUC1 EXPRESSION

MUC1 positivity was found as 3+ in 62.5%, ,2+ in 85.7% and 1 + in 70.6% of males ,with 66.7% of males showed negativity and in females 3+ in 37.5%, 2+ in 14.3% and 1+ in 29.4% of females ,with 33.3% of females showed negativity and a slight predominance in positivity among male population was seen . (Table 25 & Chart 15)

Table 25 Correlation Of Gender With MUC 1 Expression

			MUC1				Total
			Negative	1+	2+	3+	
Sex	Male	Number of cases	12	12	6	5	35
		MUC1 (%)	66.7%	70.6 %	85.7%	62.5%	70.0%
	female	Number of cases	6	5	1	3	15
		MUC1 (%)	33.3%	29.4 %	14.3%	37.5%	30.0%
Total		Count	18	17	7	8	50
		% within MUC1	100	100	100	100	100

Pearson Chi-Square 1.135 p>0.05 (0.769)

CORRELATION OF TUMOUR SITE WITH MUC1 EXPRESSION

In the present study, MUC1 expression of **3+** was found in 75.%, **2+** in 57.1%, **1+** in 64.7% of tumors in the pyloro antrum, **3+** in 12.5%, **2+** in 28.6% and **1+** in 29.4% of tumors in the body, **3+** in 12.5% of tumors in the fundus, and **2+** in 14.3% ,**1+** in 5.9% of tumors in OG junction . The association with respect to site was found to be significant with increased expression of MUC1 seen in the tumors located in the pyloro - antrum (Table 26 and Chart16)

Table 26 Correlation Of Tumor Site With MUC 1 Expression

			MUC1				Total
			Negative	1+	2+	3+	
site	Pyloroantrum	Number of cases	14	11	4	6	35
		MUC1 (%)	77.8 %	64.7%	57.1%	75.0%	70.0%
	Body	Number of cases	3	5	2	1	11
		MUC1(%)	16.7 %	29.4%	28.6%	12.5%	22.0%
	Fundus	Number of cases	0	0	0	1	1
		MUC1(%)	0.0%	0.0%	0.0%	12.5%	2.0%
	OG junction	Number of cases	1	1	1	0	3
		MUC1(%)	5.6%	5.9%	14.3%	0.0%	6.0%
Total		Number of cases	18	17	7	8	50
		MUC1(%)	100	100	100	100	100

Pearson Chi-Square 8.078 p>0.05 (0.526)

CORRELATION OF GROSS TYPE WITH MUC1 EXPRESSION

Among the various gross types, MUC 1 positivity 3+ was noted in 3 cases (37.5%) of Bormann type I, 1 case (12.5%) of Bormann type II, 3 cases (37.5%) of Bormann type III and 1 case (12.5%) of Bormann type IV. (Table 27 and Chart17)

Table 27-Correlation Of Gross Type With MUC1 Expression

			MUC1				Total
			Negative	1+	2+	3+	
Gross	TYPE I	Number of cases	1	1	0	3	5
		MUC1(%)	5.6%	5.9%	0.0%	37.5%	10.0%
	TYPEII	Number of cases	4	7	6	1	18
		MUC1(%)	22.2%	41.2%	85.7%	12.5%	36.0%
	TYPE III	Number of cases	9	8	1	3	21
		MUC1(%)	50.0%	47.1%	14.3%	37.5%	42.0%
	TYPE IV	Number of cases	4	1	0	1	6
		MUC1(%)	22.2%	5.9%	0.0%	12.5%	12.0%
Total		Number of cases	18	17	7	8	50
		MUC1(%)	100	100	100	100	100

Pearson Chi-Square 19.138* $p<0.05$ (0.24)

CORRELATION OF TUMOUR SIZE WITH MUC1 EXPRESSION

In the present study, MUC1 positivity 3+ was noted in an increased frequency (87.5%) in cases with tumor size >5cm compared to the 12.5% of cases with size <5cm. (Table 28 and Chart 18)

Table 28 Correlation Of Tumor Size With MUC1 Expression

			MUC1				Total
			Negative	1+	2+	3+	
size	<5cm	Count	6	9	4	1	20
		MUC1 (%)	33.3%	52.9%	57.1%	12.5%	40.0%
	>5cm	Count	12	8	3	7	30
		MUC1(%)	66.7%	47.1%	42.9%	87.5%	60.0%
Total		Count	18	17	7	8	50
		MUC1(%)	100	100	100	100	100

Pearson Chi-Square 4.898 p>0.05 (0.179)

CORRELATION OF HISTOLOGICAL TYPE WITH MUC1

Among histological forms, 50% of tubular carcinomas, 12.5% of papillary carcinoma, 37.5% of diffuse carcinomas and 66.7% of diffuse carcinomas showed **3+** positivity for MUC1. 85% of tubular carcinomas, 14.3% of papillary carcinomas showed **2 +** positivity for MUC1. 76.5% of tubular carcinomas, 11.8% of papillary carcinoma, 5.9 % of Diffuse carcinomas and 5.9% of mucinous carcinomas showed **1+** positivity for MUC1. 83.3% of tubular carcinomas, 11.1% of papillary carcinoma, 0% of Diffuse carcinomas and 5.6% of mucinous carcinomas showed negativity for MUC1. (Table 29and Chart 19)

Table 29 Correlation Of Histological Type With MUC1

			MUC1				Total
			Negative	1+	2+	3+	
Histological_type	Tubular	Number of cases	15	13	6	4	38
		MUC1(%)	83.3%	76.5%	85.7%	50.0%	76.0%
	Papillary	Number of cases	0	2	1	1	4
		MUC1(%)	0.0%	11.8%	14.3%	12.5%	8.0%
	Diffuse	Number of cases	2	1	0	3	6
		MUC1(%)	11.1%	5.9%	0.0%	37.5%	12.0%
	Mucinous	Number of cases	1	1	0	0	2
		MUC1 (%)	5.6%	5.9%	0.0%	0.0%	4.0%
Total		Number of cases	18	17	7	8	50
		MUC1(%)	100	100	100	100	100

Pearson Chi-Square 9.792 p>0.05 (0.368)

CORRELATION OF LAUREN'S CLASSIFICATION WITH MUC1 EXPRESSION

When Lauren's classification was taken into account, a greater frequency of MUC1 expression **3+** was seen with 62.5% ,**2+** in 100% , **1+** in 94.1% of Intestinal type cancers in comparison with **3+** in 37.5%, **2+** in 0%, **1+** in 5.9% of diffuse type carcinomas (Table 30 and Chart 20)

Table 30 - Correlation Of Lauren's Classification With MUC1 Expression

			MUC1				Total
			Negative	**1+**	**2+**	**3+**	
Lauren	Intestinal type	Number of cases	17	16	7	5	45
		MUC1 (%)	94.4%	94.1%	100.0 %	62.5%	90.0%
	Diffuse type	Number of cases	1	1	0	3	5
		MUC1 (%)	5.6%	5.9%	0.0%	37.5%	10.0%
Total		Number of cases	18	17	7	8	50
		MUC1 (%)	100	100	100	100	100

Pearson Chi-Square 8.215* $p<0.05$ (0.042)

CORRELATION OF TUMOUR GRADE WITH MUC1 EXPRESSION

An increasing percentage of cases showing MUC1 **3+** Positivity with increasing tumor grade was observed. 1 2.5% of moderately differentiated tumors (G2) and 87.5% of poorly differentiated tumors (G3) showing **3+** positivity for MUC1 was observed. 0% of well differentiated tumors showed MUC1 **3+** positivity (Table 31 and Chart 21)

Table 31 Correlation Of Tumor Grade With MUC1 Expression

			MUC1				Total
			Negative	**1+**	**2+**	**3+**	
Grade	1	Number of cases	6	1	0	0	7
		MUC1(%)	33.33%	5.88%	0.00%	0.00%	14.00%
	2	Number of cases	10	9	5	1	25
		MUC1(%)	55.56%	52.94%	71.43%	12.50%	50.00%
	3	Number of cases	2	7	2	7	18
		MUC1(%)	11.11%	41.18%	28.57%	87.50%	36.00%
Total		Number of cases	18	17	7	8	50
		MUC1(%)	100	100	100	100	100

Pearson Chi-Square 17.965 p *<0.05 (0.048)

CORRELATION OF T STAGE WITH MUC1 EXPRESSION

According to the T stage, 0% of T2 cases, 62.5% of T3 cases and 37.5% of T4 cases showing **3+** positivity for MUC1 was noted. (Table 32 and Chart 22)

Table 32 Correlation Of T Stage With MUC1 Expression

			MUC1				Total
			Negative	1+	2+	3+	
Depth	T2	Number of cases	6	2	0	0	8
		MUC1(%)	33.3%	11.8%	0.0%	0.0%	16.0%
	T3	Number of cases	11	11	5	5	32
		MUC1(%)	61.1%	64.7%	71.4%	62.5%	64.0%
	T4	Number of cases	1	4	2	3	10
		MUC1(%)	5.6%	23.5%	28.6%	37.5%	20.0%
Total		Number of cases	18	17	7	8	50
		MUC1(%)	100	100	100	100	100

Pearson Chi-Square 9.524 p>0.05 (0.146)

CORRELATION OF N STAGE WITH MUC 1EXPRESSION

In this study,12. 5% of N0 cases, 62.5% of N1 cases and 25% of N2 Cases show MUC1 **3+** positivity.. (Table 33 and chart 23)

Table 33 Correlation Of N Stage With MUC 1 Expression

			MUC1				**Total**
			-	**1+**	**2+**	**3+**	
LN	N0	Number of cases	9	8	4	1	22
		MUC1(%)	50.0%	47.1%	57.1%	12.5%	44.0%
	N1	Number of cases	8	8	2	5	23
		MUC1(%)	44.4%	47.1%	28.6%	62.5%	46.0%
	N2	Number of cases	1	1	1	2	5
		MUC1(%)	5.6%	5.9%	14.3%	25.0%	10.0%
Total		Number of cases	18	17	7	8	50
		MUC1(%)	100	100	100	100	100

Pearson Chi-Square 5.784 p>0.05 (0.448)

CORRELATION OF TNM STAGE WITH MUC1 EXPRESSION

MUC1 positivity **3+** was noticed in 0% of stage I cases,12.5% of stage II

Table 34 -Correlation Of TNM Stage With MUC1 Expression

			MUC1				Total
			Negative	1+	2+	3+	
stage	IB	Number of cases	4	2	0	0	6
		MUC1(%)	22.2%	11.8%	0.0%	0.0%	12.0%
	II	Number of cases	6	5	3	1	15
		MUC1(%)	33.3%	29.4%	42.9%	12.5%	30.0%
	IIIA	Number of cases	7	6	2	2	17
		MUC1(%)	38.9%	35.3%	28.6%	25.0%	34.0%
	IIIB	Number of cases	0	1	1	2	4
		MUC1(%)	0.0%	5.9%	14.3%	25.0%	8.0%
	IV	Number of cases	1	3	1	3	8
		MUC1(%)	5.6%	17.6%	14.3%	37.5%	16.0%
Total		Number of cases	18	17	7	8	50
		MUC1(%)	100	100	100	100	100

Pearson Chi-Square 13.377 p>0.05 (0.342)

cases,50% of stage III cases and 37.5% of stage IV cases.**2+** in 0% of stage I cases,42.9% of stage II cases,42.9% of stage III cases and 14.3% of stage IV cases. **1+** in 11.8% of stage I cases, 29.4% of stage II cases,41.2% of stage III cases and 17.6 % of stage IV cases (Table 34 and Chart 24)

CORRELATION OF MUC1 WITH OTHER PROGNOSTIC PARAMETERS

In this study, MUC1 **3+** Positivity was observed in 25% of cases with lymphovascular invasion, 25% of cases with perineural invasion and 12.5% of cases having lymphocytic infiltration. (Table 35 & chart 25)

Table 35- Correlation Of MUC1 With Other Prognostic Parameters

			MUC1				Total
			Negative	1+	2+	3+	
Lymphovascular invasion	Absent	Number of cases	13	8	3	6	30
		MUC1(%)	72.2%	47.1%	42.9%	75.0%	60.0%
	Present	Number of cases	5	9	4	2	20
		MUC1(%)	27.8%	52.9%	57.1%	25.0%	40.0%
Total		Number of cases	18	17	7	8	50
Perineural invasion	Absent	Number of cases	16	13	7	6	42
		MUC1(%)	88.9%	76.5%	100.0%	75.0%	84.0%
	Present	Number of cases	2	4	0	2	8
		MUC1(%)	11.1%	23.5%	0.0%	25.0%	16.0%
Total		Number of cases	18	17	7	8	50
Lymphocytic infiltration	Absent	Number of cases	12	9	5	7	33
		MUC1(%)	66.7%	52.9%	71.4%	87.5%	66.0%
	Present	Number of cases	6	8	2	1	17
		MUC1(%)	33.3%	47.1%	28.6%	12.5%	34.0%
Total		Number of cases	18	17	7	8	50

The present study showed that there was statistically significant association between MUC1 expression and Bormann gross typing and Lauren's histological typing and Histological tumor grading. MUC1 positive expression was seen to increase with increasing age and intestinal type of gastric adenocarcinomas.

But when subjected to statistical analysis this association was not found to be significant with age. Increased MUC1 expression was noted in Bormann type III and type IV tumor.

Chart 1-Age Wise Distribution Of Gastric Carcinoma

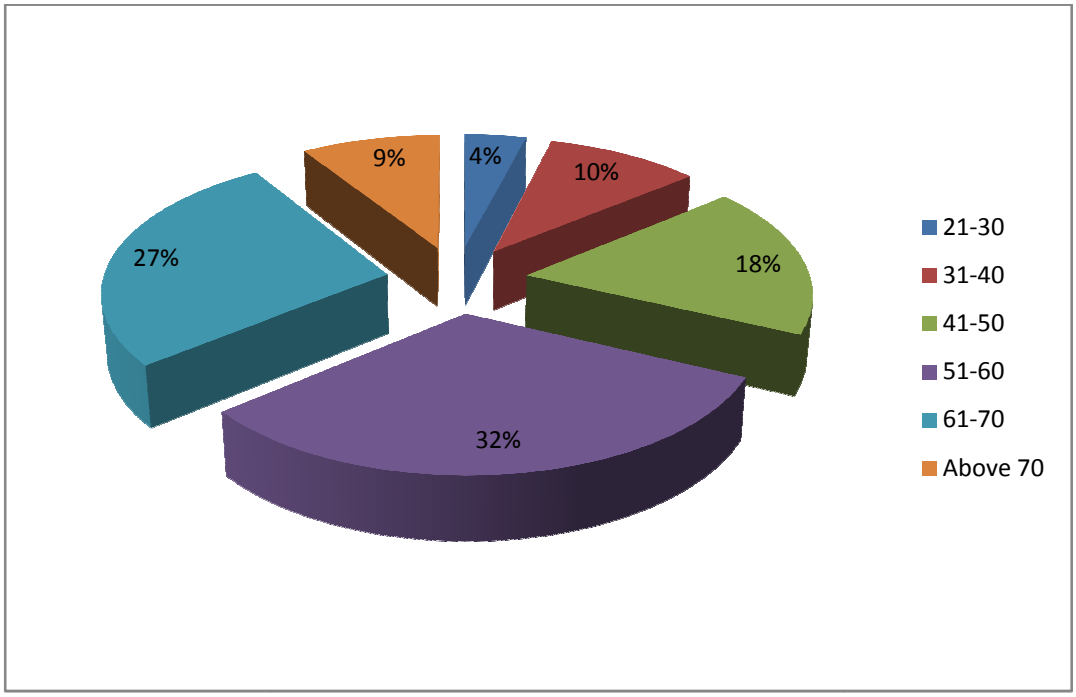


Chart 2- Sex Wise Distribution in Gastric Carcinoma

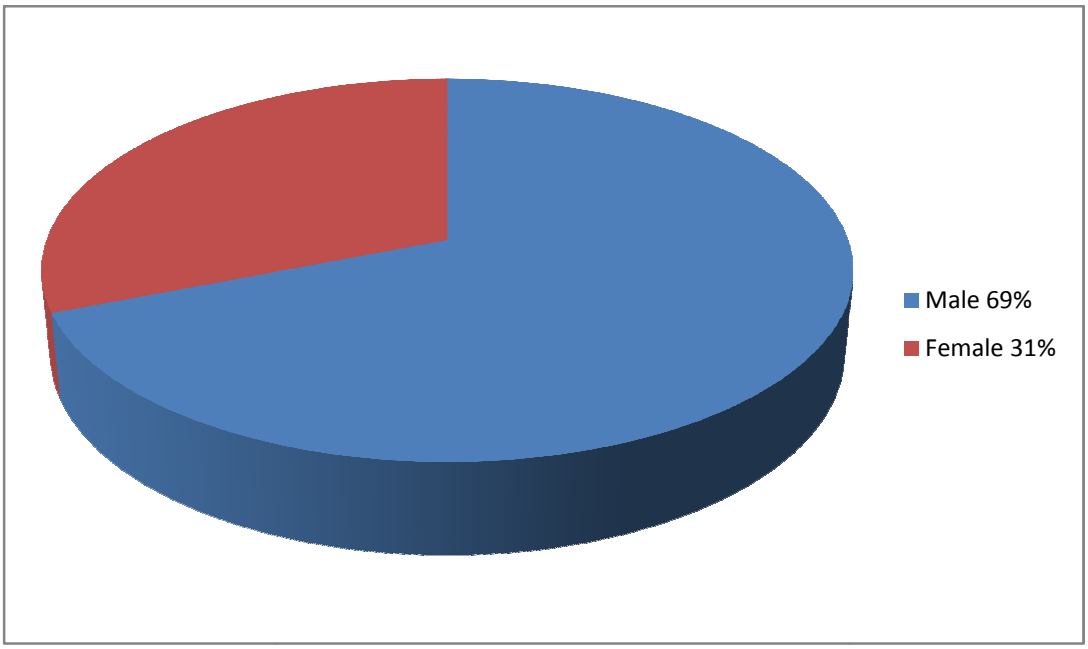


Chart 3- Distribution Of Site Of Involvement Of Gastric Cancer

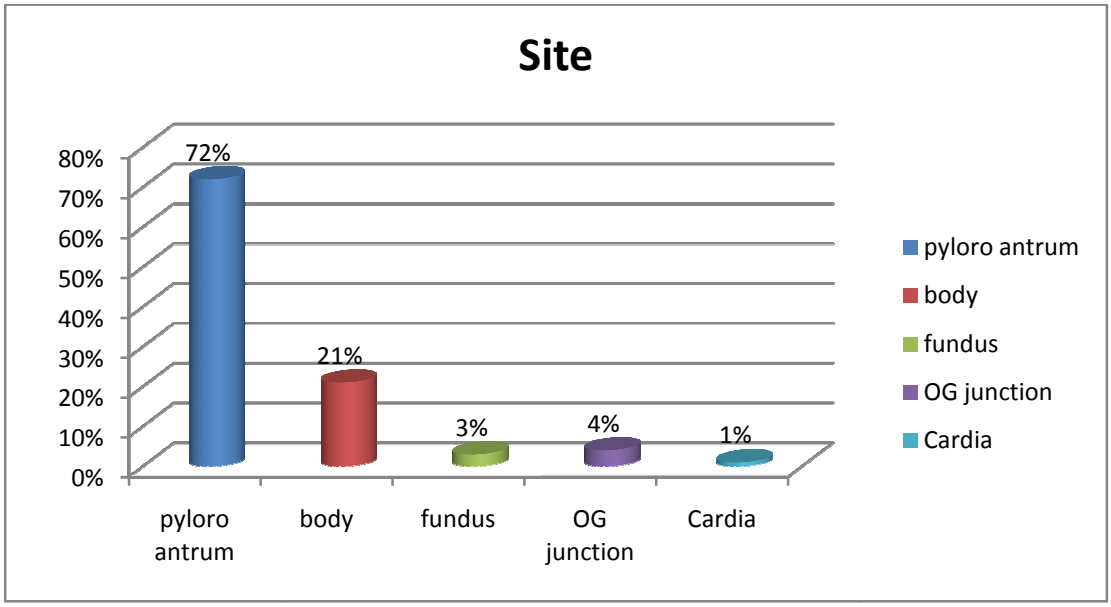


Chart 4 -Distribution Of Gastric Carcinoma According To Gross (Bormann)

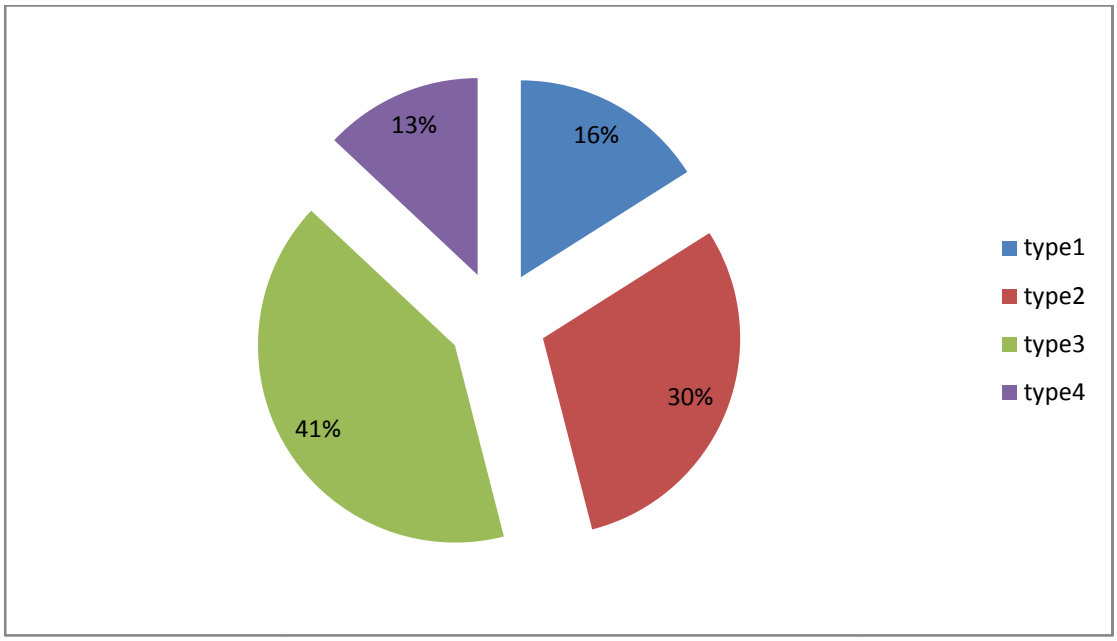


Chart 5- Distribution Of Size (Cm) In Gastric Carcinoma

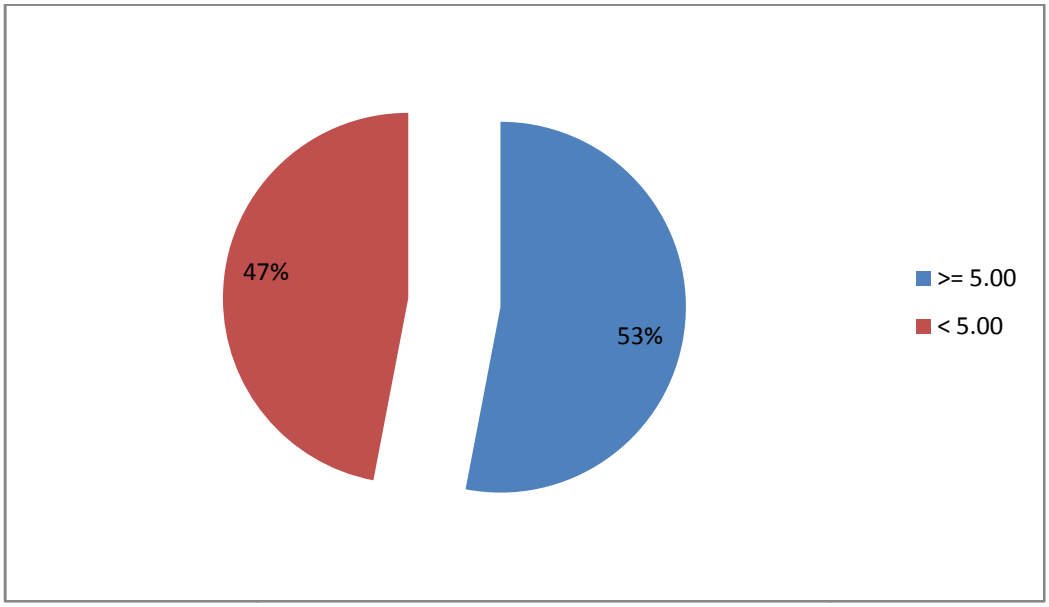


Chart 6-Distribution Of Histological Subtypes In Gastric Cancers

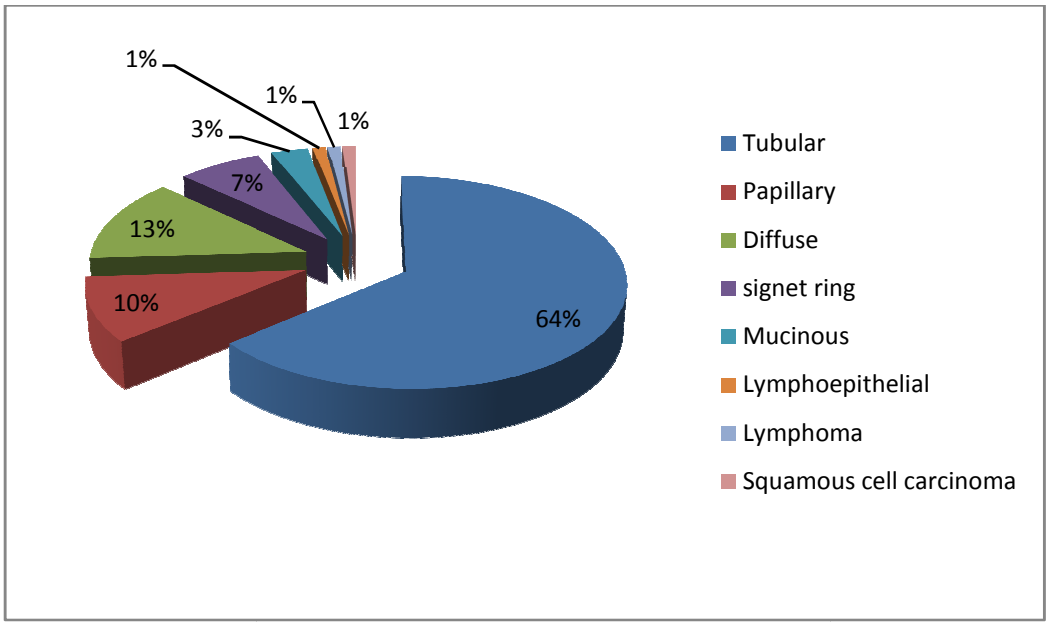


Chart 7- Distribution Of Gastric Carcinoma According To Lauren's Classification

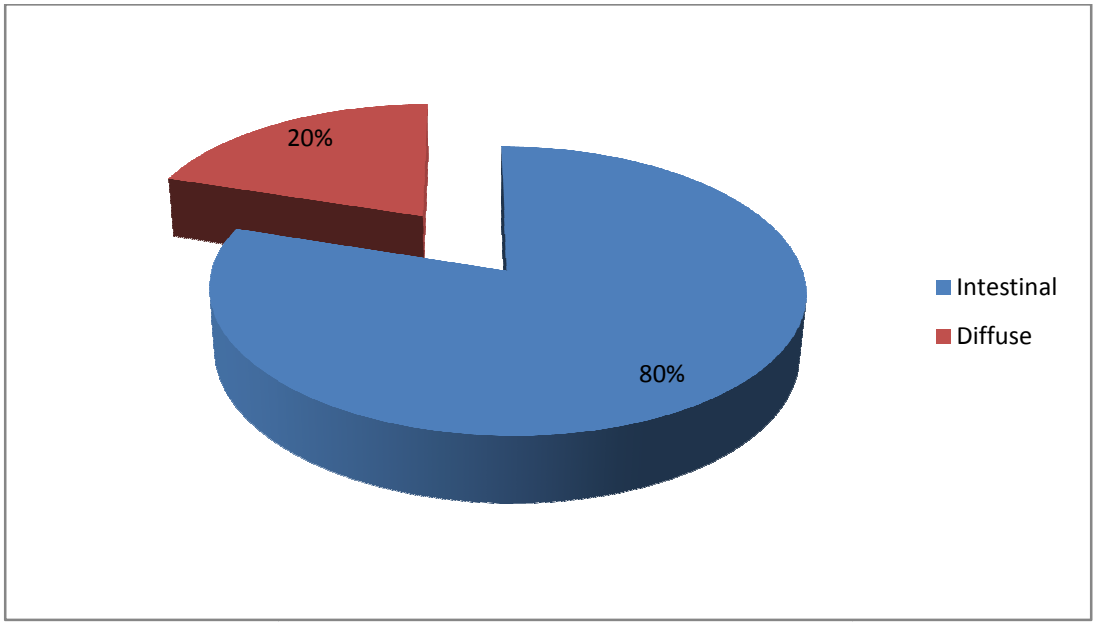


Chart 8- Distribution Of Gastric Carcinoma According To Histological Grading

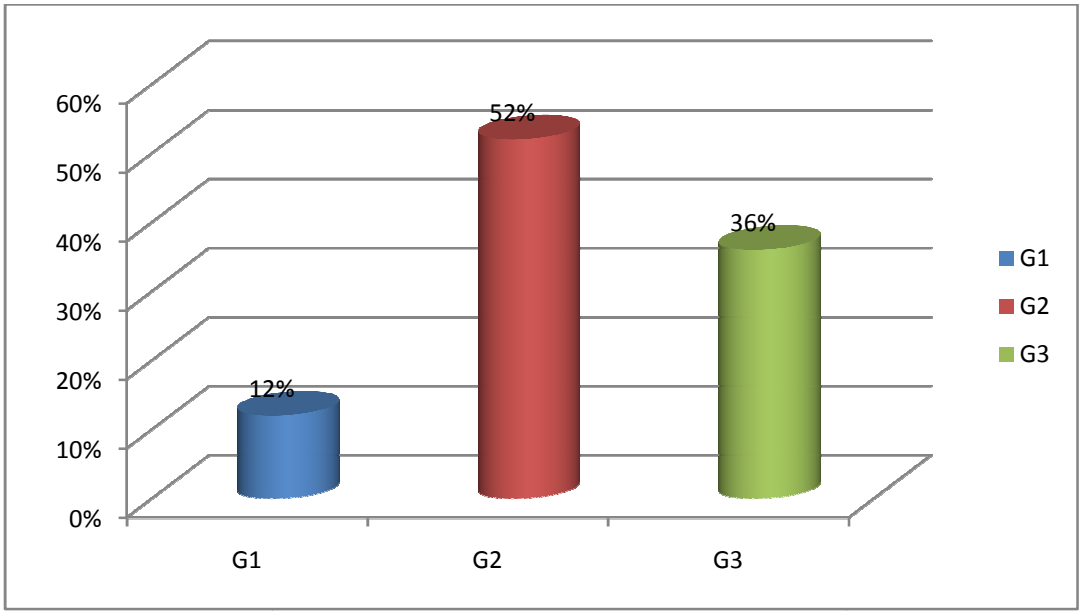


Chart 9- Distribution Of Gastric Carcinoma According To Depth Of Invasion

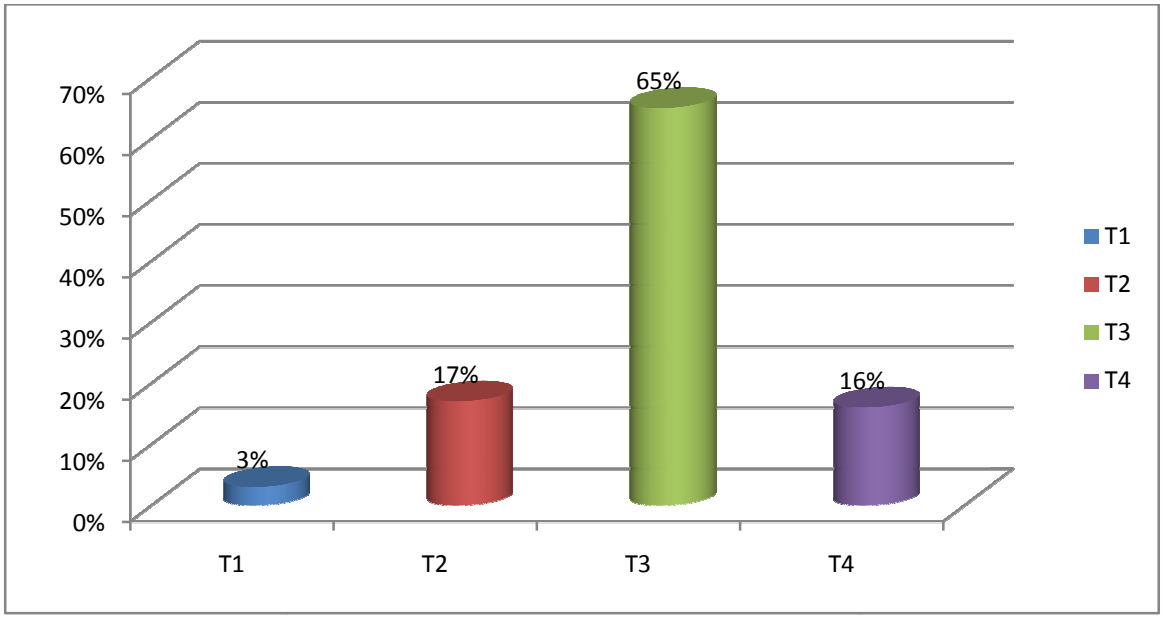


Chart 10 Distribution Of Nodal Metastasis In Gastric Cancer

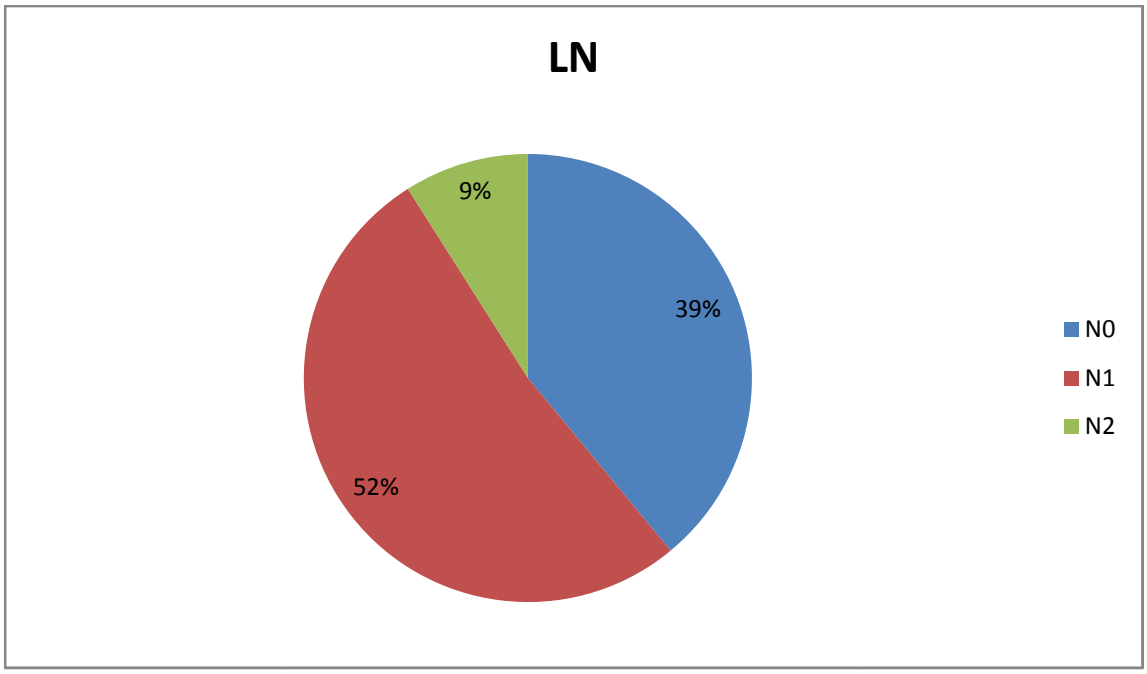


Chart 11- Distribution Of Gastric Carcinomas According To Stage

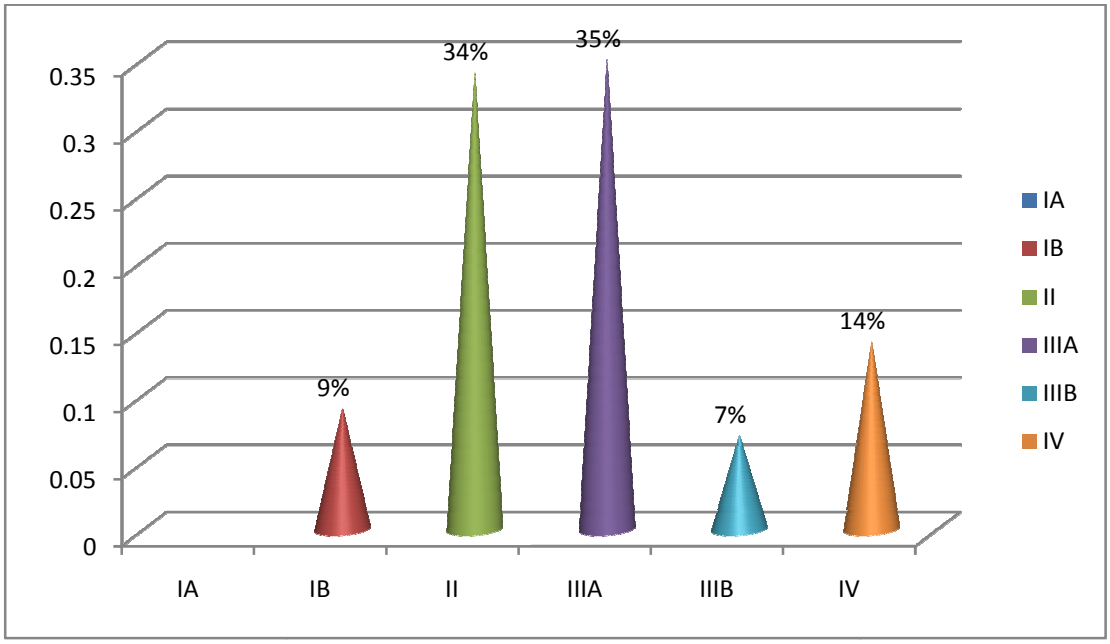


Chart 12-istribution Of Other Prognostic Factors In Gastric Carcinoma

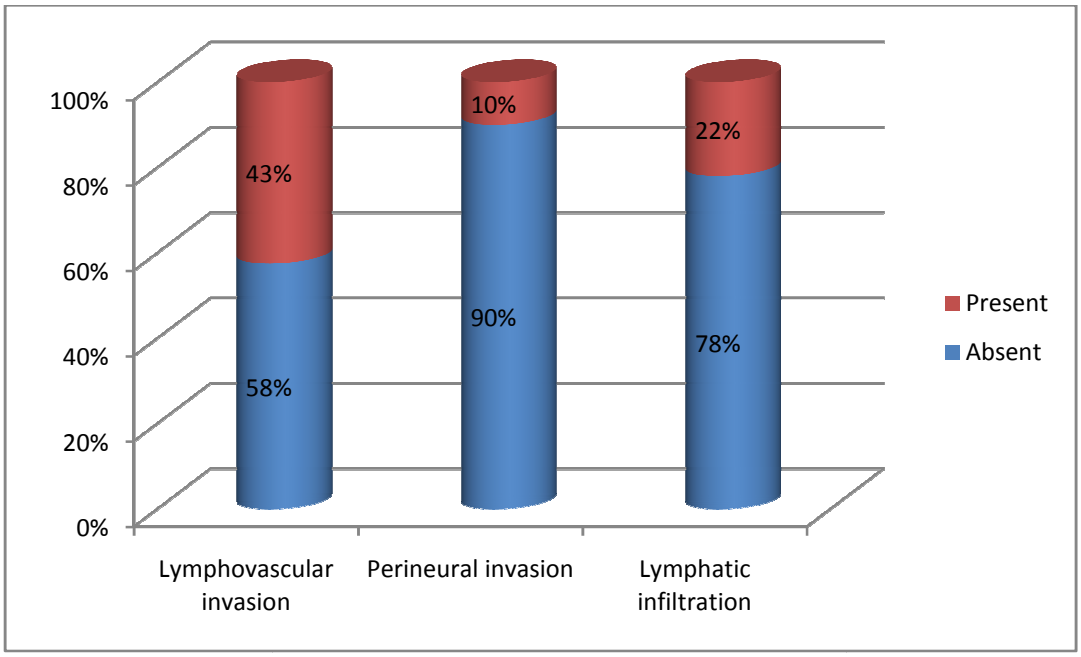


Chart 13– Distribution Of MUC1 In Gastric Carcinoma

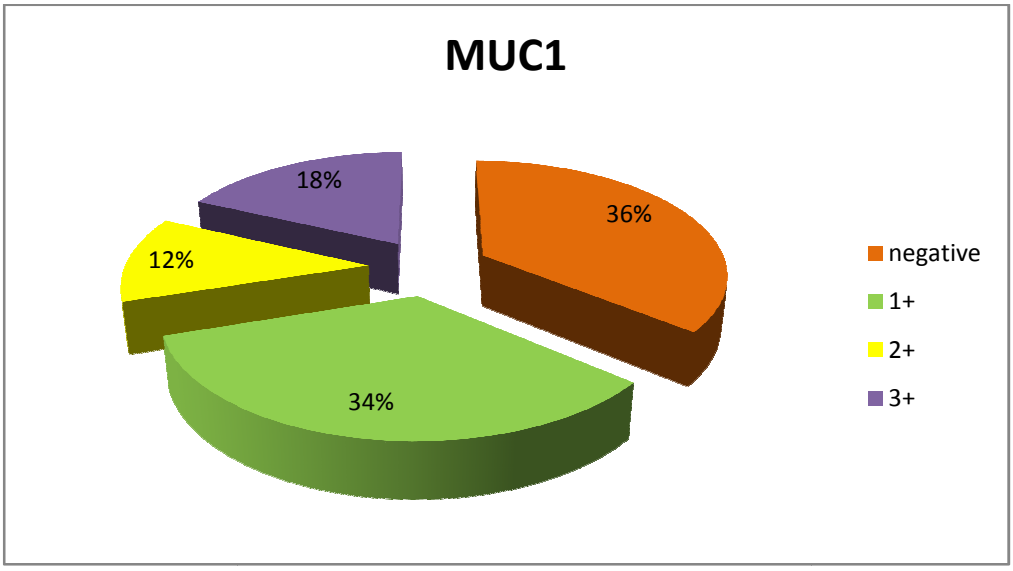


Chart 14- Correlation Of Age With MUC1 Expression

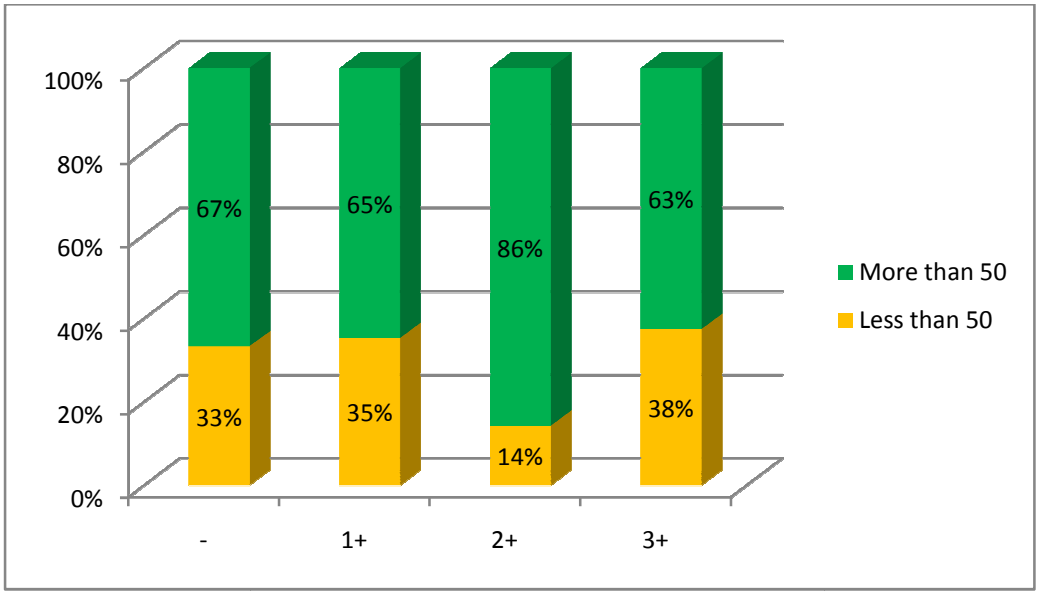


Chart 15- Correlation Of Gender With MUC1 Expression

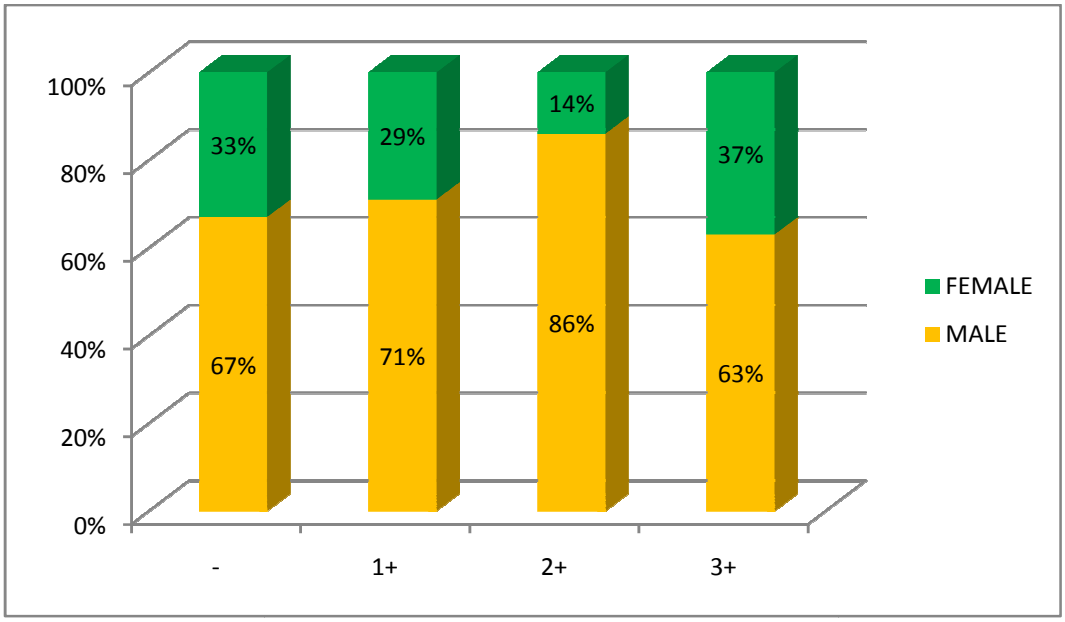


Chart 16- Correlation Of Tumor Site With MUC1 Expression

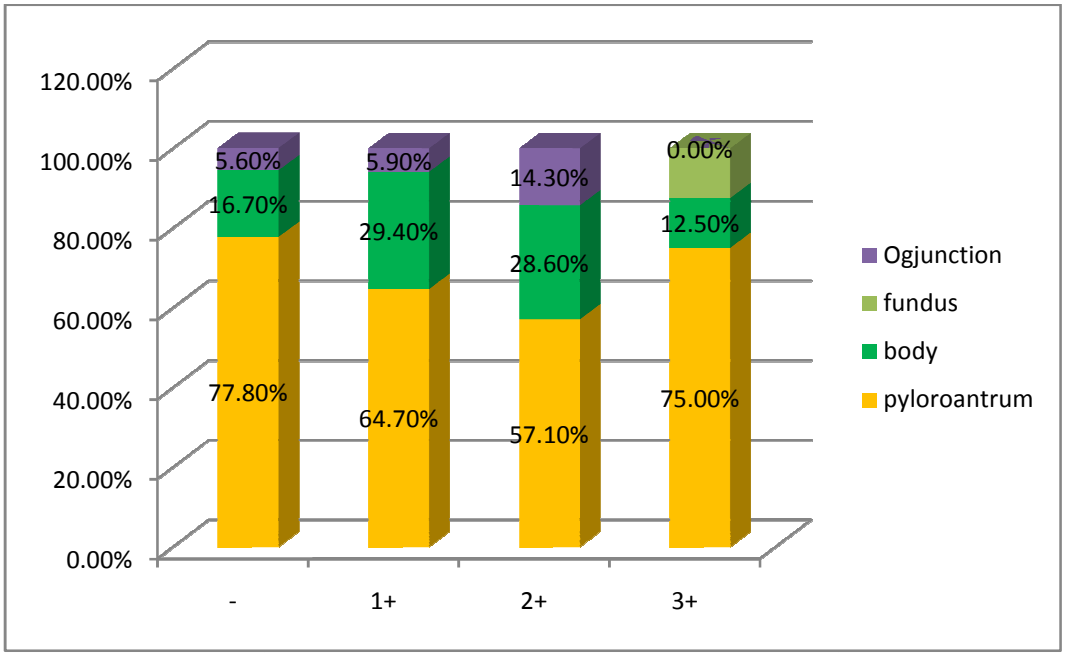


Chart 17 -Correlation Of Gross Type With MUC1 Expression

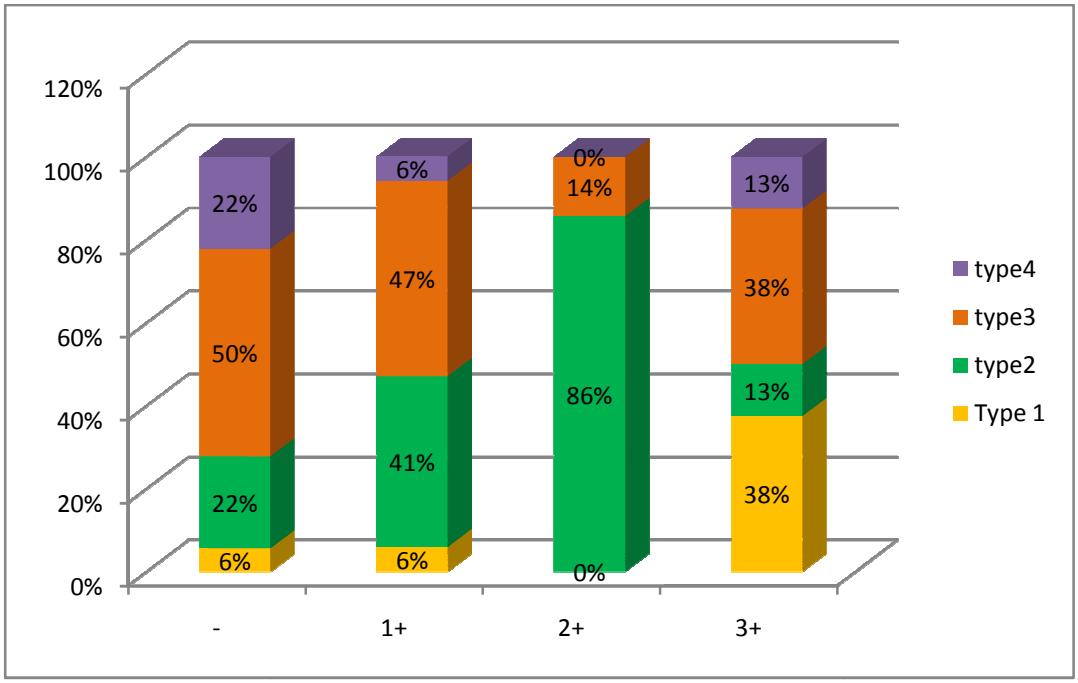


Chart 18 Correlation Of Tumor Size With MUC1 Expression

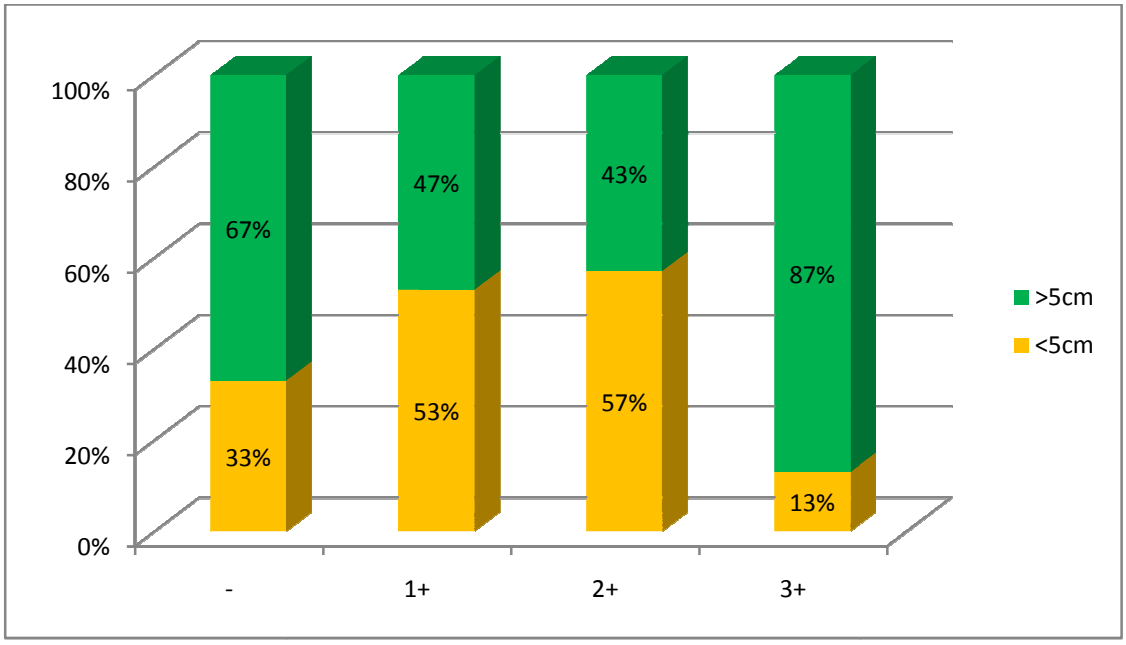


Chart19 Correlation Of Histological Type With MUC1

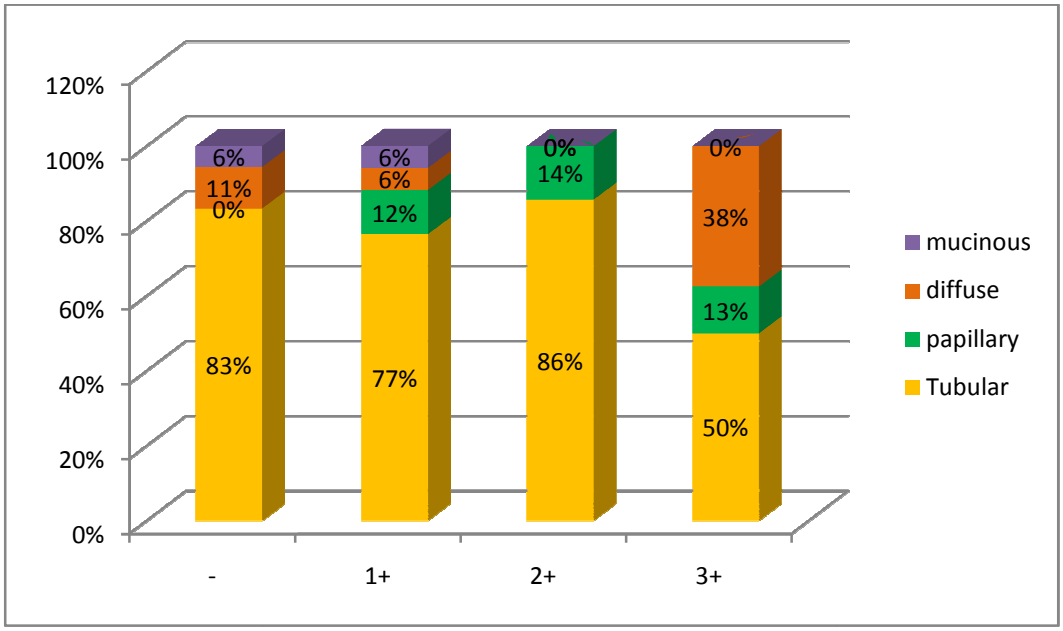


Chart 20-Correlation Of Lauren's Classification With MUC1 Expression

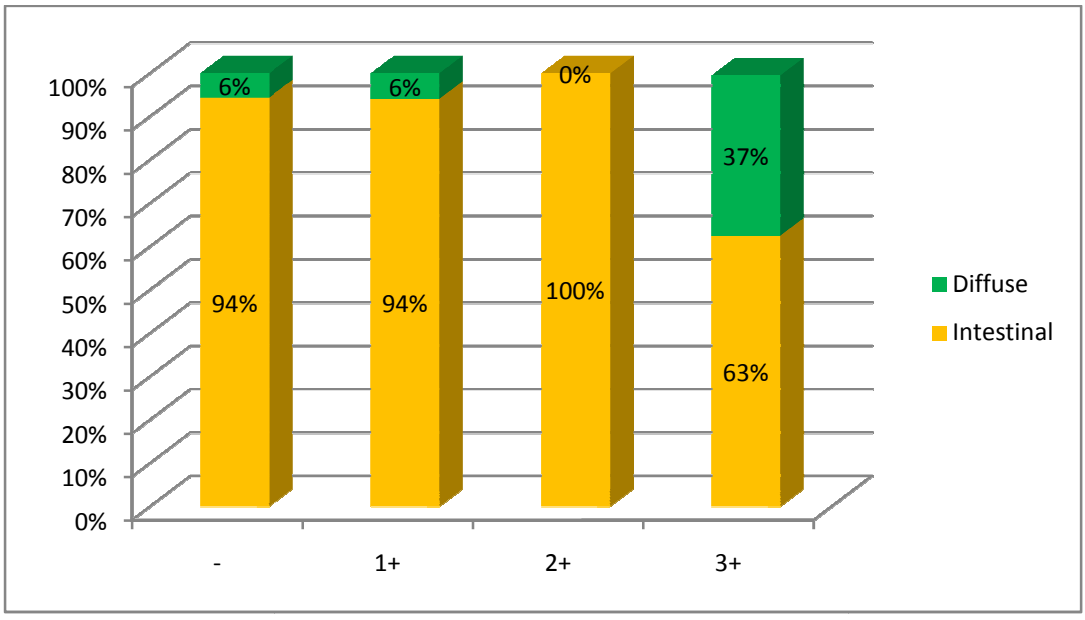


Chart 21-Correlation Of Tumor Grade With MUC1 Expression

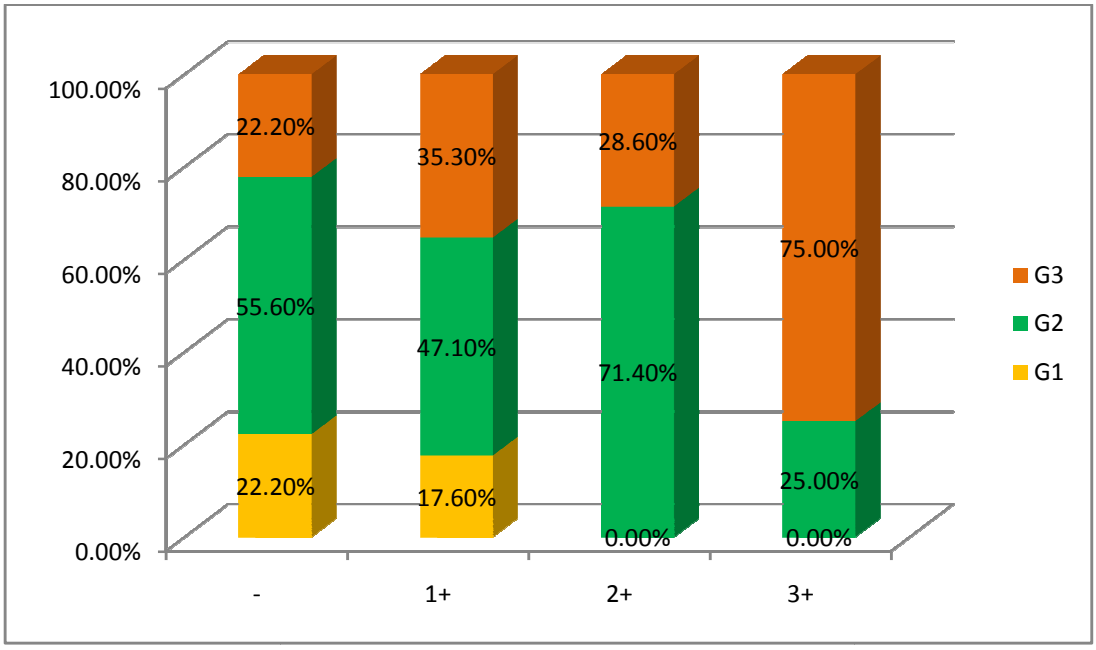


Chart 22 Correlation Of T Stage With MUC1 Expression

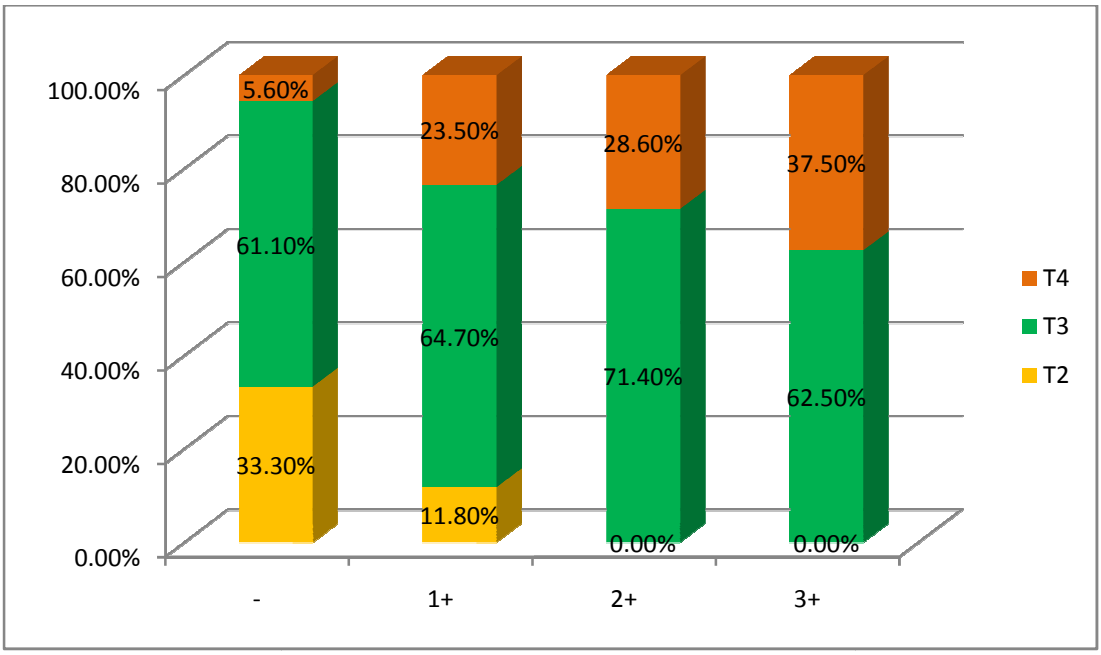


Chart23 Correlation Of N Stage With MUC 1 Expression

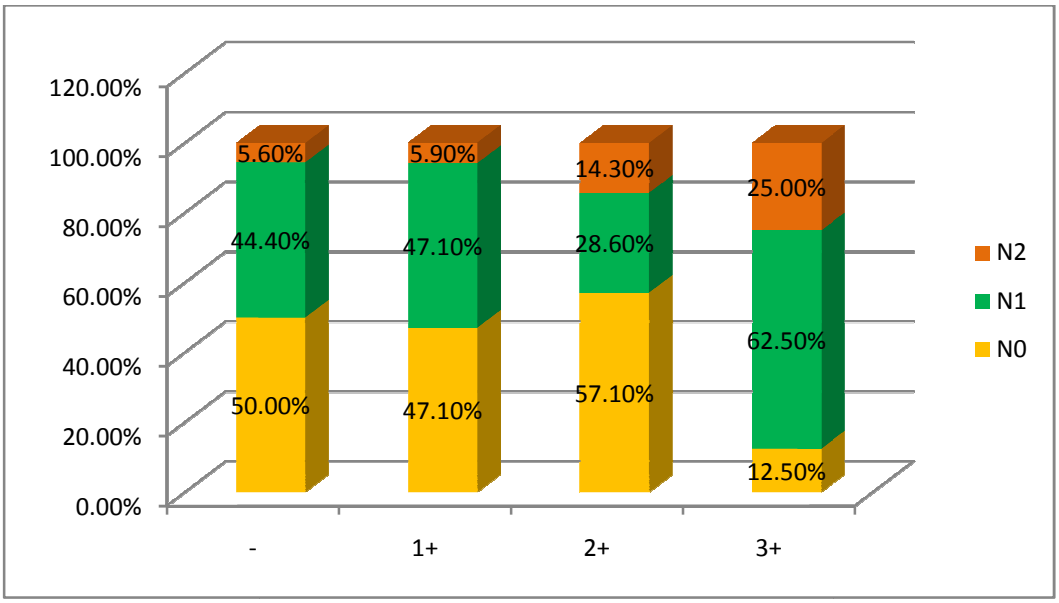


Chart 24-Correlation Of TNM Stage With MUC1 Expression

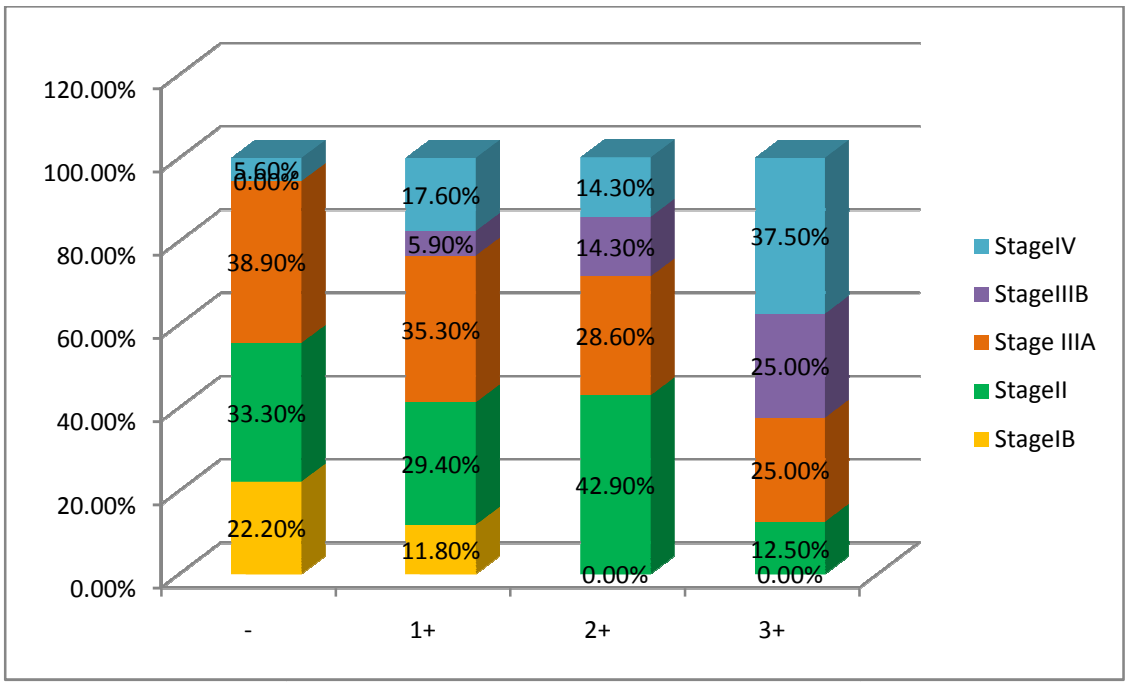
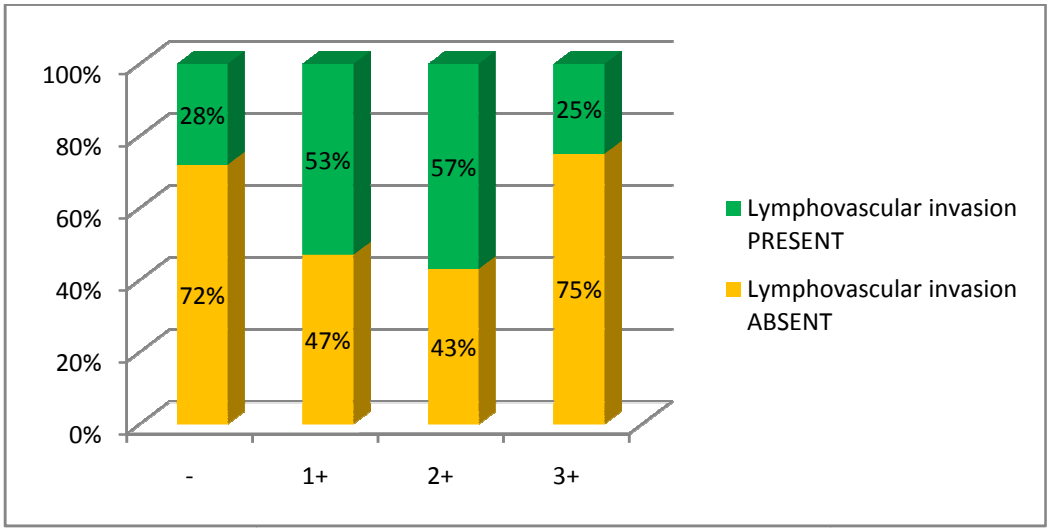
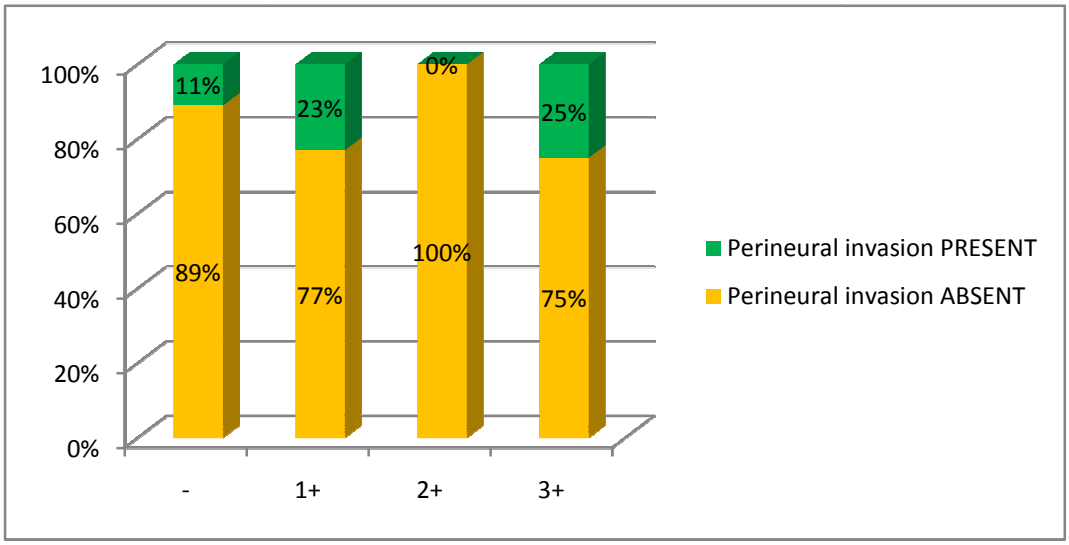


Chart25- Correlation Of MUC1 With Other Prognostic Parameters





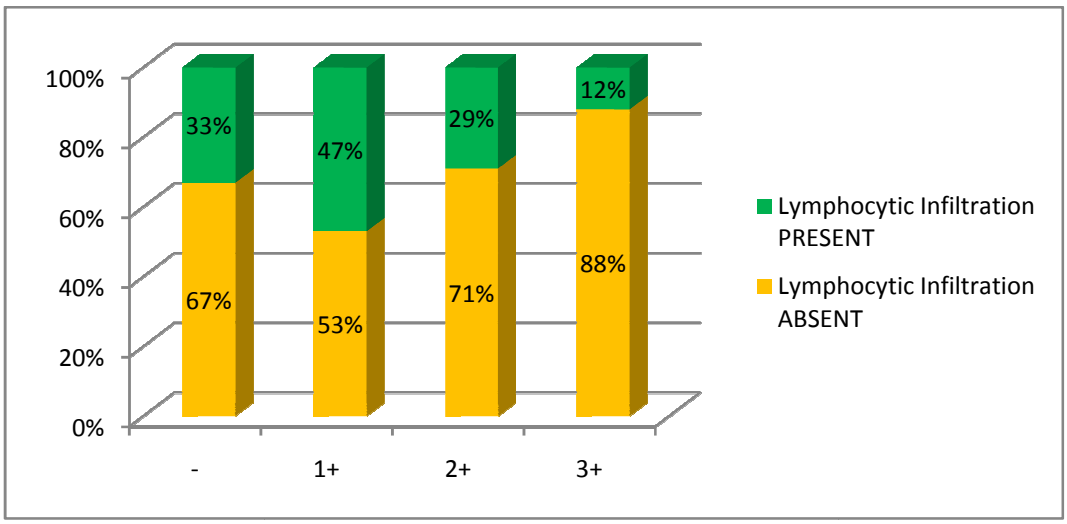


Figure 1: HPE-3865 / 15 GASTRIC CARCINOMA-ULCERATIVE GROWTH

Figure 2: HPE 4648/15 GASTRIC CARCINOMA CIRCUMFERENTIAL ULCERATIVE GROWTH

Figure 3:HPE4846/15GASTRIC CARCINOMA-ULCERO PROLIFERATIVE GROWTH

Figure 4:HPE1090/15GASTRIC CARCINOMA-FLATTENED GROWTH

Figure 5: HPE 3833/15:Well differentiated gastric adeno carcinoma (10x)

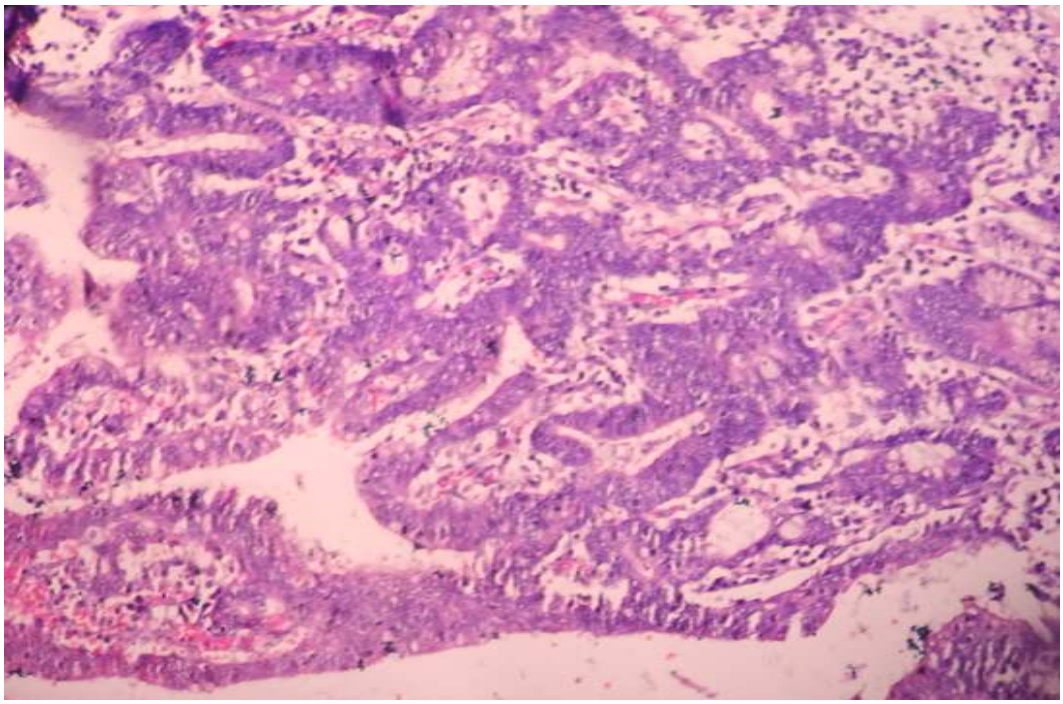


Figure 6-HPE 3833/15 IHC -MUC1 Negative

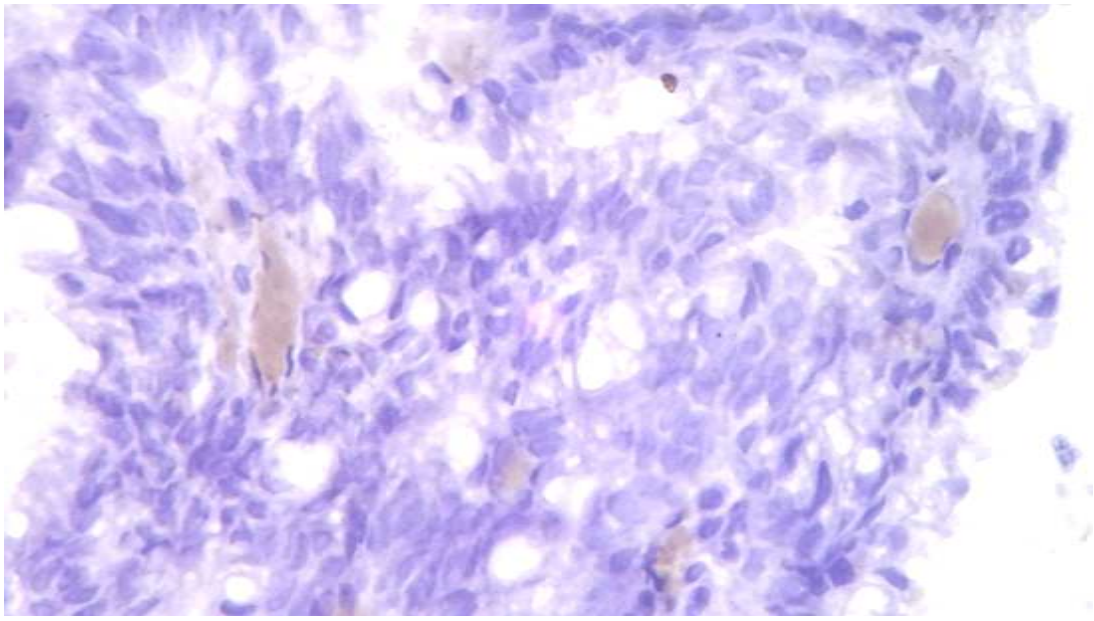


Figure 7: HPE4846/15 -Moderately differentiated gastric carcinoma (10x)

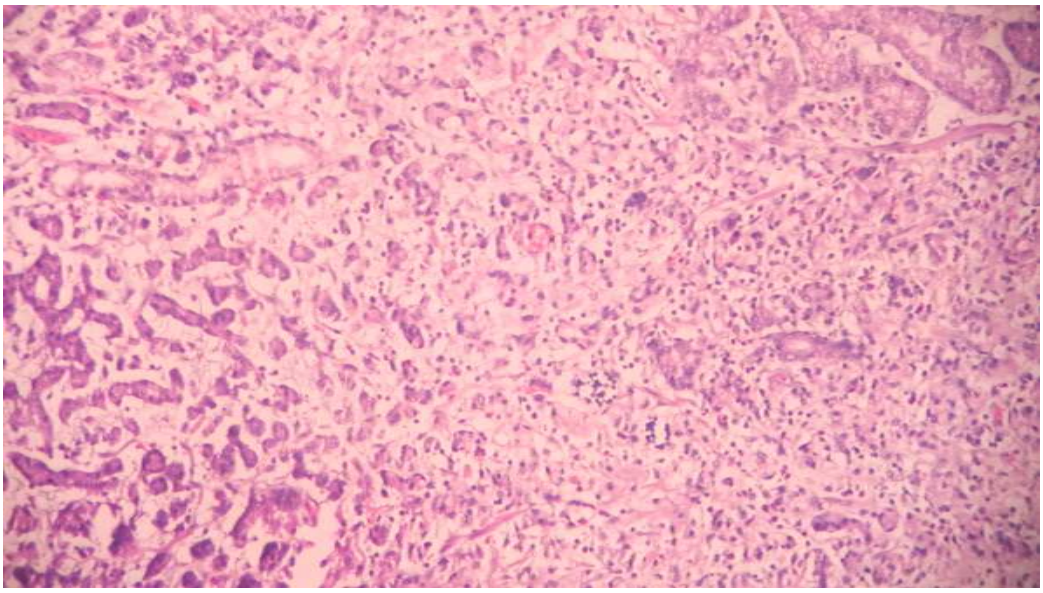


Figure 8-HPE 4846/15 IHC-MUC1 faint Positive 1+

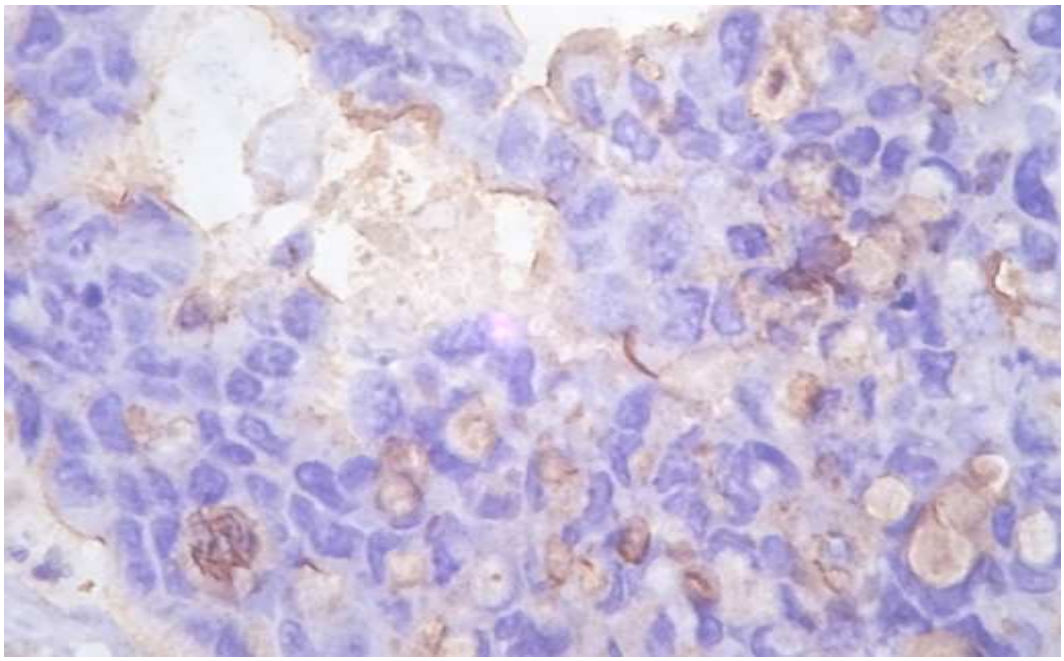


Figure 9-HPE 7350/15 Poorly differentiated gastric adenocarcinoma (40x)

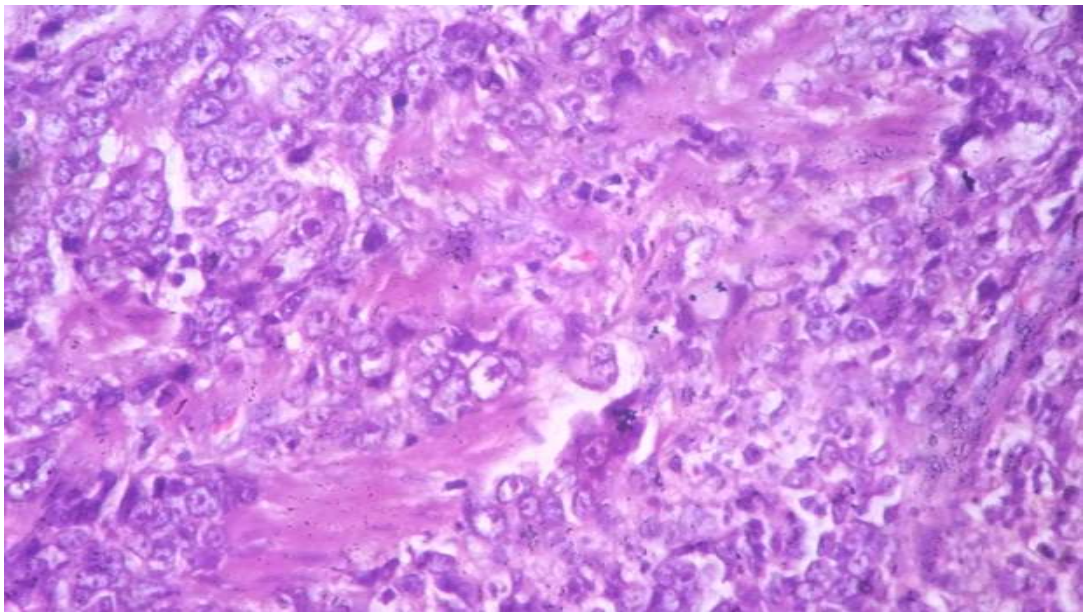


Figure 10-HPE 7350/15 IHC-MUC1 Positive 2+

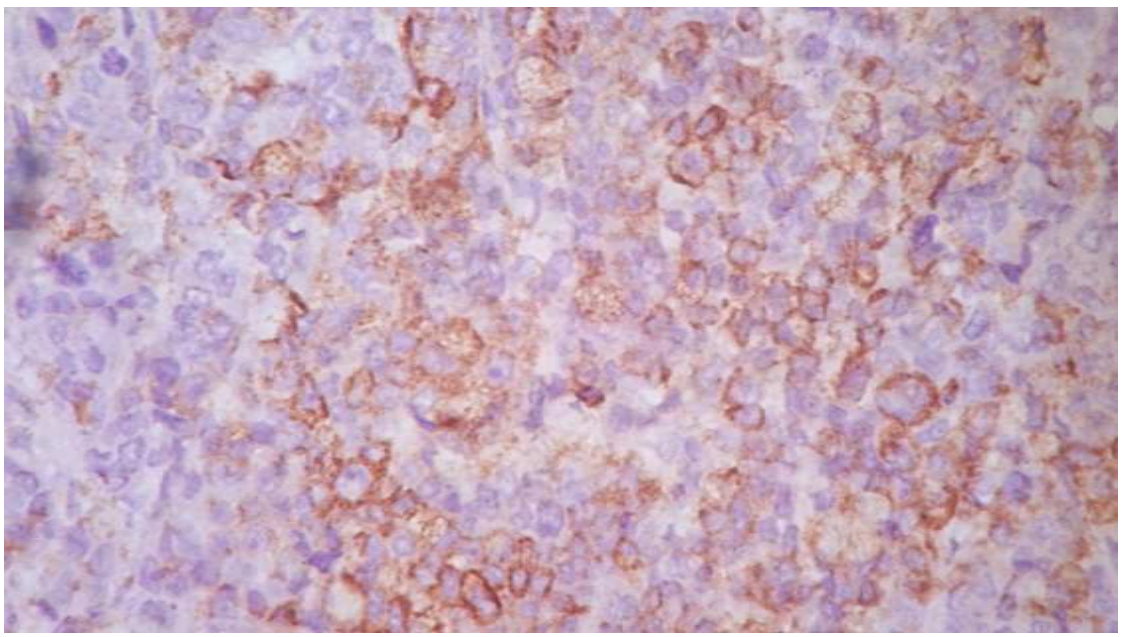


Figure 11-HPE 10869/15 Poorly differentiated gastric adenocarcinoma (40x)

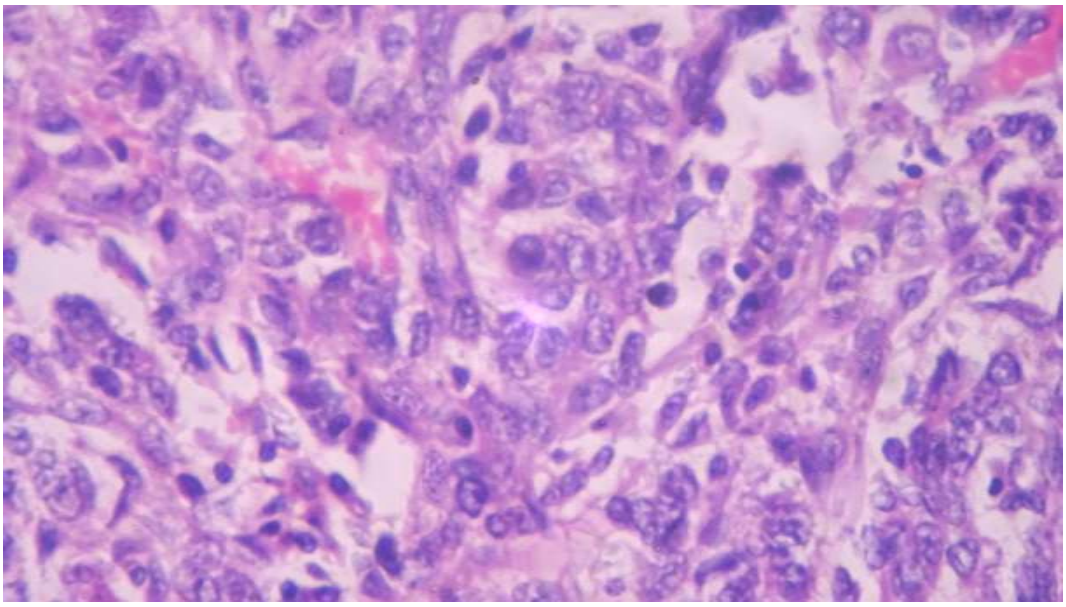


Figure 12-HPE 10869/15 IHC-MUC1 Positive 3+

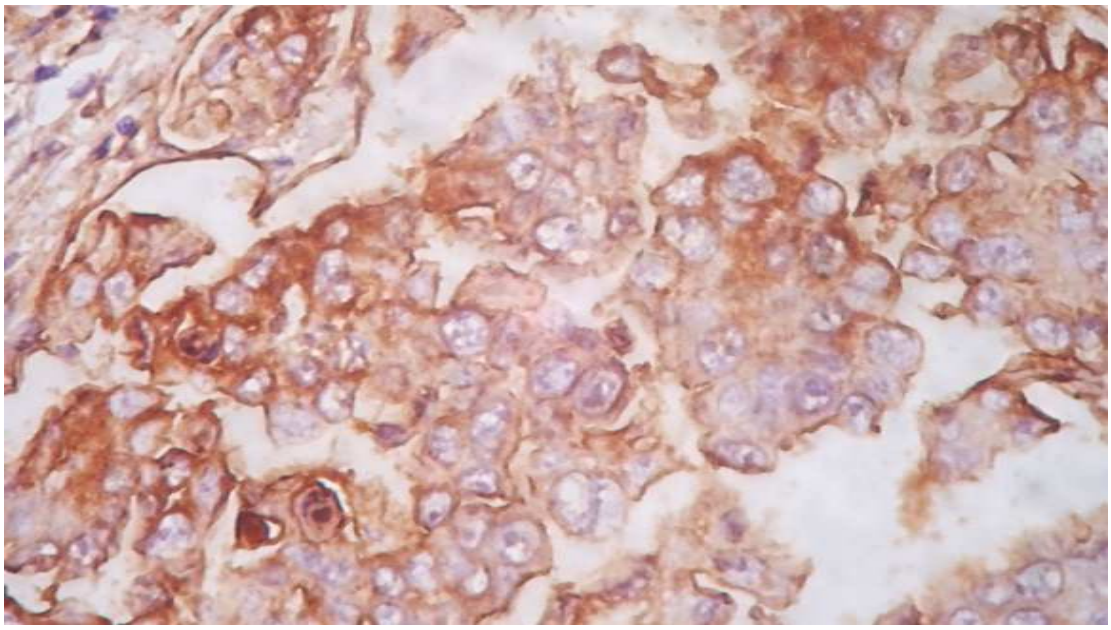


Figure 13-HPE 4572/15 well differentiated gastric adenocarcinoma

Tubular pattern with lymphocytic infiltration (10x)

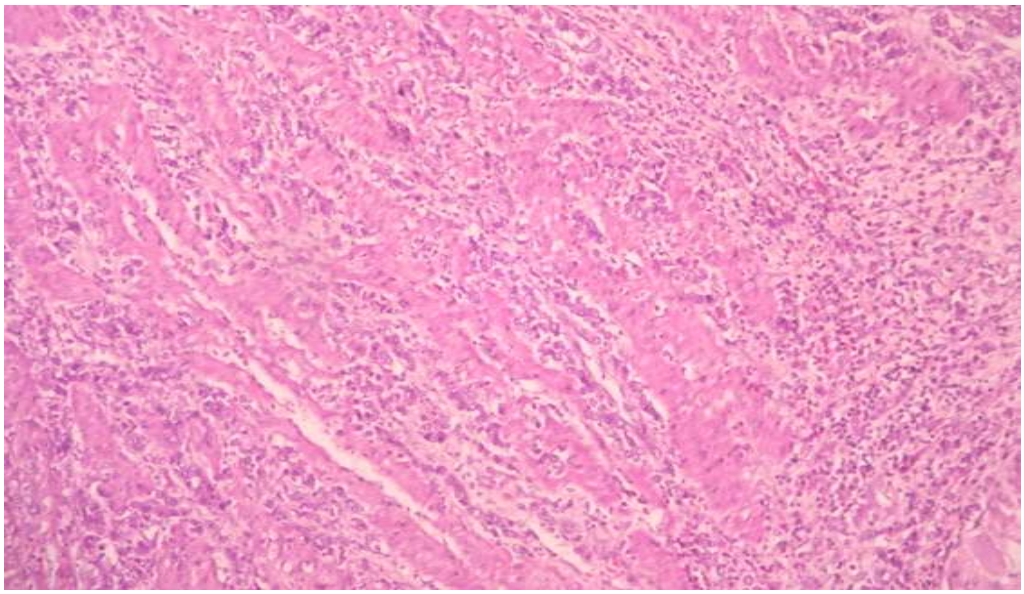


Figure 14-HPE 11361/14 poorly differentiated gastric adenocarcinoma

Lympho vascular invasion (10x)

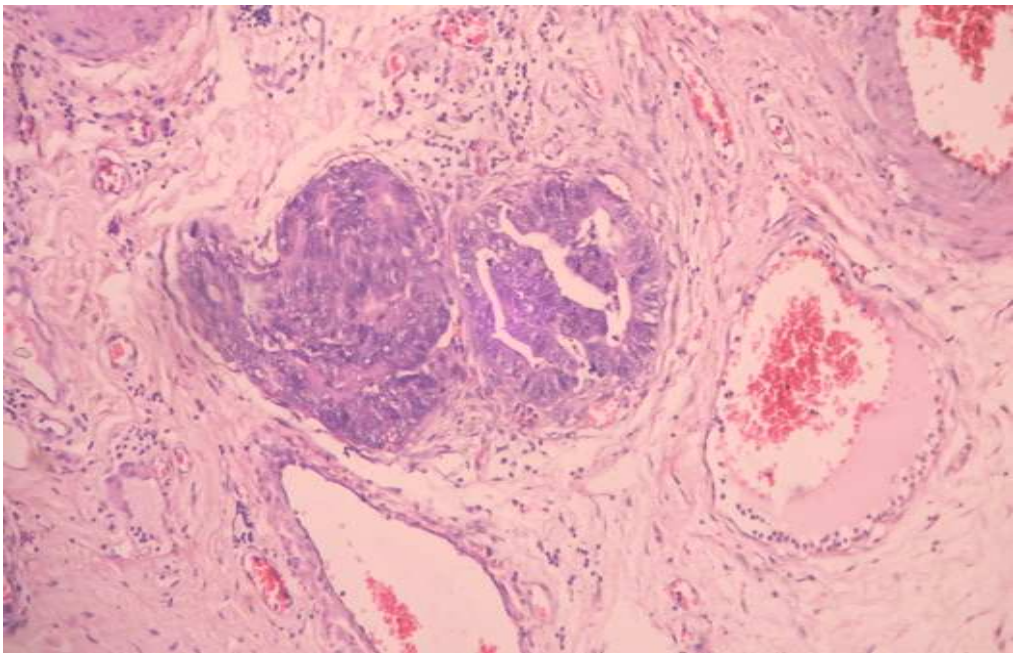


Figure 15-HPE 11361/14 poorly differentiated gastric adenocarcinoma

Lymphocytic infiltration with foci of necrosis (10x)

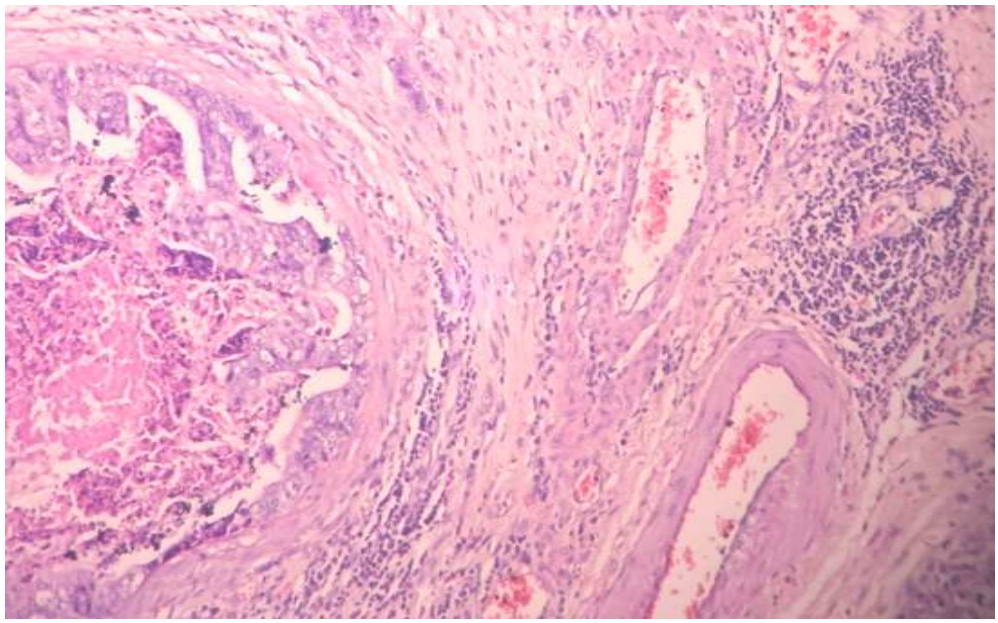
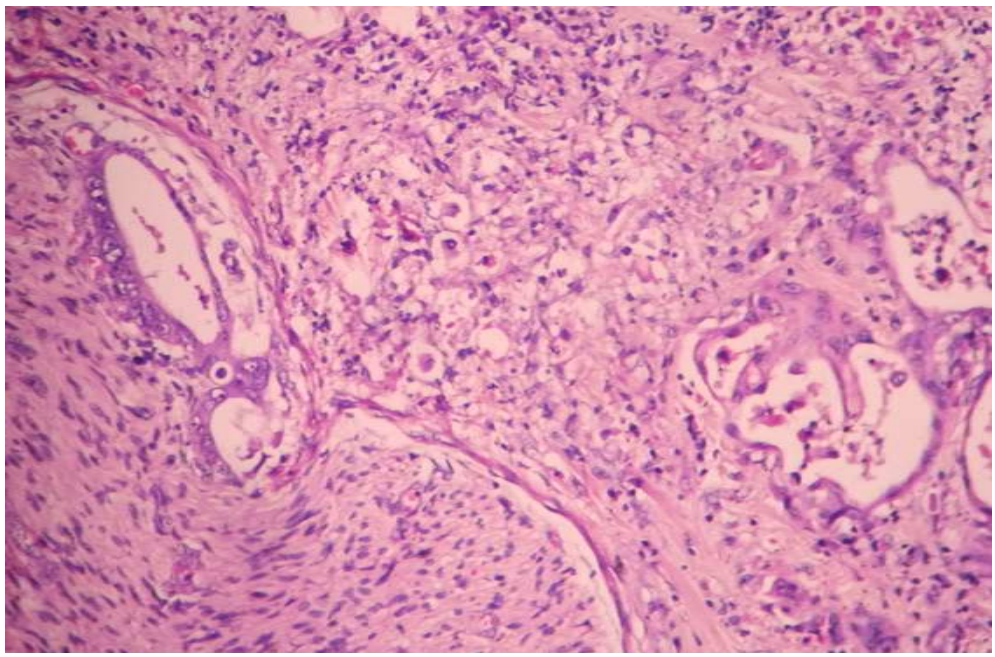


Figure 16 -HPE 10869/14 poorly differentiated gastric adenocarcinoma

Perineural invasion (10x)



DISCUSSION

Gastric cancer is a life threatening disease and represents a significant health problem worldwide. It is the second most common cancer worldwide and the third most common cancer in India[73]. The incidence of gastric cancer in Chennai is about 13.6 per lakh in men and 6.5 per lakh in women[20]

Many biological markers have been examined as possible tools for the evaluation of the biological behavior of gastric cancer in order to predict the clinical outcome. Among these, immunohistochemical staining of MUC1 have been proposed to be of significant value.

In the present study, immunohistochemical evaluation was done in 50 cases of gastric carcinomas and an attempt was made to correlate the MUC1 expression with the known prognostic factors of gastric cancers.

This study showed the age of gastric cancer patients ranged from 20 years to 78 years with the mean age of 55 years. The highest incidence of gastric cancer occurred in 51 to 60 year age group. This is in concurrence with the study done by Y.E. Joo et al who observed a mean age of 58.7 years with a range from 28 to 79 years. In the study done by Nobuyuki Igarashi et al the incidence of gastric cancer in men and women was 74.1% and 25.9% respectively.

In concurrence with the above studies, a significant predominance of gastric cancers was found in men accounting for 70% of the cases and women accounting for 30% was observed.

Site

The most common site of gastric cancer in this study is the pyloro – antrum (54%). This is almost similar to the study of N.E. Tzanakis et al102 and Daniela Lazar et al[75]. In their study, Tzanakis et al[74] observed 51.6% tumours in the antrum and Daniela Lazar et al[75] observed 50.8% tumours in the antrum (Table 36).

TABLE 36 – COMPARISON OF DISTRIBUTION OF GASTRIC TUMOUR LOCATION

Tumour location	N.E.Tzanakis et al[74]	Daniela Lazar et al[75]	Czyzewska J et al[79]	Current study
Antrum	51.6%	50.8%	60%	70%
Body	34.4%	24.5%	20%	22%
Fundus	14%	13.1%	15.6%	2%
OG junction	-	11.4%	4.4%	6%

Bormann type

Daniela Lazar et al[75] observed 8.2% of Bormann type I tumors, 32.7% of type II tumors, 36% of type III tumors and 14.7% of type IV tumors. Jurgen et al[76] observed 20% of type I tumors, 40% of type II tumors, 28% of type III tumors and 12% of type IV tumors. Similar findings were also observed by Jurgen et al[76]. In the current study 10% of Bormann type I, 36 % of Bormann type II, 42% of Bormann type III and 12% of Bormann type IV (table 37).

Table 37

Tumour location	Daniela Lazar et al[75]	Jurgen et al[76]	Current study
Type I	8.2%	20%	10%
TypeII	32.7%	40%	36%
Type III	36%	28%	42%
Type IV	14.7%	12%	12%

Size

In this study, an average tumor size of 5 cm was observed which was similar to the findings observed by Y.E.Joo[77] et al and Tzanakis et al[74]. Y.E Joo et al observed an average tumour size of 5.2 cm and Tzanakis et al[74] observed an average tumour size of 5.1 cm (table 38).

Table 38

Tumor size	Y.E.Joo et al[77]	Tzanakis et al[74]	Current study
In cm	5.2	5.1	5

Histological subtype

The most common histological subtype of gastric cancer in this study is Tubular carcinoma. This is almost similar to the study of Daniela Lazar et al[75] and Y.Kakeji et al[78] (Table 39).

TABLE 39 – COMPARISON OF DISTRIBUTION OF HISTOLOGICAL TYPES OF GASTRIC CARCINOMA

Histological type	Daniela et al[75]	Y.Kakeji et al[78]	Current study
Tubular carcinoma	45.9%	89.5%	76%
Papillary carcinoma	8.2%	2%	8%
Diffuse carcinoma	4.9%	-	12%
Mucinous carcinoma	27.8%	3.1%	4%

Lauren's histological type

The most common histological type (Lauren's) in this study was the Intestinal type (82%). This is similar to observations made by Casasola et al106 wherein, intestinal type accounted for 81.9% and diffuse type accounted for 18.1% (Table 40).

TABLE 40– COMPARISON OF LAUREN'S HISTOLOGICAL TYPE

Lauren's type	Czyzewska et al[79]	Daniela et al[75]	Casasola et al[80]	Current study
Intestinal type	75.5%	72.1%	81.9%	90%
Diffuse type	24.5%	27.9%	18.1%	10%

Histological Grading

In the present study, the G2 (moderately differentiated) tumors were more common than the other grades of distribution. This was in concurrence with the study conducted by Casasola et al[80] (Table 41).

TABLE 41 – COMPARISON OF GRADE OF TUMOUR

Grade	Casasola et al[80]	Tzanakis et al[74]	Daniela et al[75]	Current study
G1	16%	5.4%	3.2%	14%
G2	74.6%	22.6%	32.8%	50%
G3	9.4%	69.9%	64%	36%

Depth of tumor

A higher proportion of T3 tumors, closely followed by T2 tumors were observed in this study, similar to the studies of Giovanni de Manzoni et al[81], and Y.E. Joo[77] et al (Table 42).

TABLE –42 COMPARISON OF DEPTH OF TUMOUR

Depth	T1	T2	T3	T4
Giovanni et al[81]	-	25%	66%	9%
Y.E.Joo et al[77]	13.4%	24.3%	51.2%	11.1%
Daniela et al[75]	6.5%	14.7%	27.8%	49.2%
Jurgen et al[76]	16.9%	36.6%	38.6%	7.9%
Current study	-	16%	64%	20%

Nodal status

There was nodal metastasis in 56% of the cases and no nodal metastasis in 44% of cases. This was similar to the study by Y.E Joo et al [77]who (table 43)

TABLE 43 – COMPARISON OF NODAL METASTASIS

Nodal status	N0	N1	N2
Giovanni et al[81]	21.4%	35.7%	42.9%
Daniela et al[75]	29.5%	26.2%	37.8%
Jurgen et al[76]	32.4%	22%	45.6%
Current study	44%	46%	10%

observed nodal metastasis in 51.3% cases and no nodal metastasis in 48.7% cases & the study by Czyzewska J et al [79]who observed nodal metastasis in 55.6% and no nodal metastasis in 44.4% (Table 44)

TNM Stage

Most of the cases presented in stage III followed closely by stage II in this study. This did not concur with the other studies which showed a predominance of stage IV tumors (Table 44)

TABLE 44 COMPARISON OF STAGE OF GASTRIC TUMOUR

Stage	Daniela et al[75]	Y.E. Joo et al[77]	Jurgen et al[76]	Current study
I	13.1%	34.4%	27.2%	12%
II	11.4%	16%	13.9%	30%
III	31.1%	31.1%	28.1%	42%
IV	42.6%	18.5%	30.8%	16%

Other parameters

40% cases had lymphovascular invasion which was not similar to the observation made by Daniela Lazar et al[75], who reported 62.3% and Ji Yoon Choi et al[82] who reported 79.35% cases with invasion in his study.There were lymphocytic infiltration in 36% and perineural infiltration in 16% of gastric carcinoma cases. This observation is parallel to the 31.7% perineural infiltration reported in the study conducted by Luo Tianhang et al [83].

The expression of MUC1 was noted as 1+,2+,3+ and _ among, 34%,14%,16% and 36% of cases respectively. This proportion is comparable with the other studies conducted by Wang Zg et al[84] in the Japanese

population, Iihan et al , Nguyen et al and these studies show MUC1 expression ranging from 24% to 90%. This fluctuation could be due to different methodologies used and to varying characteristics of the studied cases (Table 45).

TABLE 45 - COMPARISON OF MUC1 EXPRESSION WITH OTHER STUDIES

Studies	MUC1 positive	MUC1 Negative
Wang Zg et al[84]	42%	58%
IIhan et al[85]	90%	NA
Nguyen et al[86]	24%	76%
Current study	64%	36%

Wang Zg et al [84](2012) studied 292 gastric cancer cases and found no significant association between MUC1 expression with age, gender, depth of invasion, lymph node metastasis and Lauren classification.

Similar to the study of Wang Zg et al [84,] current study also show no significant association between MUC1 and the age, gender, depth of invasion, lymphnode metastasis.

And in contradictory to the study of Wang Zg et al [84] ,the present study show significant association between MUC1 expression and Lauren's histological type of gastric carcinomas.

Reis, et al[87] (2014) studied 55 cases of gastric carcinoma and found significant association between MUC1 expression with lymphatic invasion and, nodal metastasis and no significant results with advanced stage.

And In contradictory to the study of Reis, et al[87] ,the present study show no significant association between MUC1 expression and lymphatic invasion and, nodal metastasis and no significant results with advanced stage.

Utsunomiya, et al[88] (2014) studied 139 cases of gastric carcinoma and found significant association between MUC1 expression with lymphatic invasion, and no significant results with nodal metastasis and advanced stage of the tumor.

The present study correlated with the study of Utsunomiya, et al [88] in which there was no significant results with nodal metastasis and stage of the tumor with the MUC1 expression.

Kocer et al[89] (2014) studied 35 cases of gastric carcinoma and found significant results with MUC1 expression and Lauren's histological classification of gastric carcinoma.

The present study correlated with the study of Kocer, et al[89] in which there was significant results with MUC1 expression and Lauren's histological classification of gastric carcinoma.

SUMMARY

- Gastric cancers had a peak incidence in the age group of 51 – 60 years, with the mean age of 55.5 years.

- 70% cases of gastric cancer were reported in males and 30% in females.

- The most common location of gastric cancer was at the pyloro - antrum which constituted about 71.7% of the cases.

- 53% of tumors were more than or equal to 5 cm.

- The most common histological type was tubular carcinoma which accounted for 64.2%of cases.

- The most common Lauren's histological subtype was Intestinal carcinoma which accounted for 79.5% of cases.

- G2 (moderately differentiated grade) was the most common grade accounting for 51.7 % of cases.

- 64.7 % of cases presented in T3 (invasion into the serosa) stage.

- Nodal metastasis was observed in 61.1% of cases.

- Most of the tumours (41.2%) presented in stage III.

- Lymphovascular invasion was seen in 42.5% of cases.

- Perineural infiltration was seen in 10% of cases.

- Lymphocytic response was seen in 21.7% of cases

- MUC 1 expression was seen in 64% of cases. 1+ in 34%, 2+ in 14% and 3+ in 16% of cases

- An increase in MUC1 (3+) positivity expression was seen with increasing age and intestinal type of gastric adenocarcinoma.

- MUC1 expression showed statistically significant association with tumor gross Bormann typing , Laurens histological Classification and Histological grading of the tumor.

- No statistically significant association between MUC1 expression and age, gender, tumor size, depth, stage, vascular invasion, perineural infiltration and lymphocytic infiltration was found.

CONCLUSION

The incidence of gastric carcinoma was higher in this study group than the western population. Many patients presented in older age with predominance in males. MUC1 expression was found in 64% of cases which is similar to that of western population. MUC1 expression was significantly associated with Bormann gross typing, Lauren's histological classification and grading of the tumor. MUC1 mucin , positivity was seen to increase with increasing age, nodal stage and TNM stage. But when subjected to statistical analysis this association was not found to be significant. There was a slight predominance in males when compared to females and intestinal type tumors than diffuse type gastric carcinomas

To conclude, the role played by MUC1 marker in the aggressiveness of gastric carcinoma is complex and still not clarified. However, identifying the expression of MUC1 in gastric carcinoma could be helpful to identify a group of patients at high risk and poor survival. A larger sample size and in concordance with other proliferation markers and close follow up of these patients for 5 or more years could be helpful in utilizing MUC1 as an aid in long term prognosis and therapeutic approach of the high risk patients.

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ANNEXURE – I

PROFORMA

Case number : Name :

HPE number : Age :

IP number : Sex :

Clinical history :

Risk factors, if any :

Clinical diagnosis :

Imaging :

Endoscopy :

Previous HPE report:

Nature of specimen : Total gastrectomy/Subtotal gastrectomy/Others

GROSS

Proximal circumference : Greater curvature:

Distal circumference : Lesser curvature :

Tumour site :

Tumour size :

Tumour configuration : Depth of invasion:

Margins : Proximal : Distal :

Associated findings :

Total nodes dissected :

MICROSCOPY

Histological type

Histological grade : G1 / G2 / G4 / G4

Depth of invasion :

Margins : Proximal : Free / Involved

Distal : Free / Involved

Lymphatic invasion : Present / Absent

Venous invasion : Present / Absent

Perineural invasion : Present / Absent

Lymphocytic response : Present / Absent

Necrosis : Present / Absent

Associated findings:

Total number of nodes dissected: Number of nodes involved:

Distant metastasis :

TNM staging :

IMMUNOHISTOCHEMISTRY

MUC1 score :

% of tumour nuclei showing reaction

ANNEXURE II

TNM STAGING OF GASTRIC TUMOURS

T – Primary Tumour

TX - Primary tumour cannot be assessed
T0 - No evidence of primary tumour
Tis - Carcinoma in situ
T1 - Tumour invades lamina propria or submucosa
T2 - Tumour invades muscularis propria or subserosa
T3 - Tumour penetrates serosa without invasion of adjacent structures
T4 - Tumour invades adjacent structures

N – Regional Lymph Nodes

NX - Regional lymph nodes cannot be assessed
N0 - No regional lymph node metastasis
N1 - Metastasis in 1 to 6 regional lymph nodes
N2 - Metastasis in 7 to 15 regional lymph nodes
N3 - Metastasis in more than 15 regional lymph nodes

M – Distant Metastasis

MX - Distant metastasis cannot be assessed
M0 - No distant metastasis
M1 - Distant metastasis

STAGE GROUPING

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T1	N1	M0
	T2	N0	M0
Stage II	T1	N2	M0
	T2	N1	M0
	T3	N0	M0
Stage IIIA	T2	N2	M0
	T3	N1	M0
	T4	N0	M0
Stage IIIB	T3	N2	M0
Stage IV	T4	N1, N2, N3	M0
	T1, T2, T3	N3	M0
	Any T	Any N	

ANNEXURE - III

WHO CLASSIFICATION OF GASTRIC TUMORS

EPITHELIAL TUMORS

Intraepithelial neoplasia – Adenoma

CARCINOMA

Adenocarcinoma
Intestinal type
Diffuse type
Papillary adenocarcinoma
Tubular adenocarcinoma
Mucinous adenocarcinoma
Signet-ring cell carcinoma
Adenosquamous carcinoma
Squamous cell carcinoma
Small cell carcinoma
Undifferentiated carcinoma
Others
Carcinoid (well differentiated endocrine neoplasm)

NON-EPITHELIAL TUMORS

Leiomyoma
Schwannoma
Granular cell tumor
Glomus tumor
Leiomyosarcoma
Gastro Intestinal stromal tumor
Benign
Uncertain malignant potential
Malignant
Kaposi sarcoma
Others
Malignant lymphomas
Marginal zone B-cell lymphoma of MALT-type
Mantle cell lymphoma
Diffuse large B-cell lymphoma
Others

SECONDARY TUMORS

ANNEXURE IV

IMMUNOHISTOCHEMISTRY PROCEDURE

1. 4μ thick sections were cut from formalin fixed paraffin embedded tissue samples and transferred to gelatin-chrome alum coated slides.
2. The slides were incubated at 58ºC for overnight.
3. The sections were deparaffinized in xylene for 15 minutes x 2 changes.
4. The sections were dehydrated with absolute alcohol for 5 minutes x 2 changes.
5. The sections were washed in tap water for 10 minutes.
6. The slides were then immersed in distilled water for 5 minutes.
7. Heat induced antigen retrieval was done with microwave oven in appropriate temperature with appropriate buffer for 20 to 25 minutes.
8. The slides were then cooled to room temperature and washed in running tap water for 5 minutes.
9. The slides were then rinsed in distilled water for 5 minutes.
10. Wash with appropriate wash buffer (citrate buffer) for 5 minutes x 2 changes.
11. Apply peroxidase block over the sections for 10 minutes.
12. Wash the slides in citrate buffer for 5 minutes x 2 changes.
13. Cover the sections with power block for 15 minutes.
14. The sections were drained (without washing) and appropriate primary antibody was applied over the sections and incubated for 1 hour

15. The slides were washed in citrate buffer for 5 minutes x 2 changes.
16. The slides were covered with Super Enhancer for 30 minutes.
17. The slides were washed in citrate buffer for 5 minutes x 2 changes.
18. The slides were covered with SS Label for 30 minutes.
19. Wash in citrate buffer for 5 minutes x 2 changes.
20. DAB substrate was prepared by diluting 1 drop of DAB chromogen to 1 ml of DAB buffer.
21. DAB substrate solution was applied on the sections for 8 minutes.
22. Wash with citrate buffer solution for 5 minutes x 2 changes.
23. The slides are washed well in running tap water for 5 minutes.
24. The sections were counterstained with Hematoxylin stain for 2 seconds (1 dip).
25. The slides are washed in running tap water for 3 minutes.
26. The slides are air dried, cleared with xylene and mounted with DPX

MASTER CHART

s.no	HPE no	Age	Sex	P/D	site	Gross	Size	Histological type	Lauren	Grade	Depth	LVI	PNI	Lymph	LN	stage	MUC1
1	3424/13	47	1	1	1	3	3	1	1	2	2	A	A	A	1	2	
2	3468/13	78	2	1	1	3	2.5	1	2	2	3	A	A	A	2	4	
3	3708/13	50	1	2	1	3	7	1	1	2	3	A	A	A	2	4	
4	4191/13	56	1	1	2	3	3	2	1	2	3	P	A	A	2	4	
5	4192/13	55	1	1	1	4	4.5	3	2	3	2	A	A	P	2	3	
6	4939/13	60	1	2	1	3	7	1	1	2	3	P	A	P	2	4	
7	5222/13	70	1	2	1	4	6	3	2	3	3	A	A	A	2	4	
8	5335/13	70	1	1	3	4	5	3	2	2	3	A	A	A	1	3	
9	5641/13	41	1	4	1	1	5	4	2	3	3	P	A	A	2	4	
10	5747/13	57	1	3	1	3	5	6	_	_	3	P	A	P	2	4	
11	5828/13	38	2	1	1	1	6	7	_	_	_	A	A	A	1	_	
12	6154/13	61	1	2	2	3	7	1	1	2	1	P	A	P	2	2	
13	6952/13	41	2	1	1	4	1.5	3	2	2	3	A	A	A	1	3	
14	7045/13	35	1	1	2	4	4	3	2	3	3	P	A	A	3	5	
15	7998/13	66	1	2	1	1	3	1	1	2	4	P	A	A	2	6	
16	8091/13	50	1	1	1	3	3.5	1	1	3	3	P	A	A	2	4	
17	8307/13	57	1	2	2	3	2	1	1	2	2	A	A	A	3	4	
18	8427/13	78	1	1	1	4	8	2	1	3	2	P	A	A	2	3	
19	8468/13	64	1	1	1	1	2.5	1	1	2	3	A	A	P	2	4	
20	8603/13	65	1	2	1	3	8	1	1	2	2	P	A	A	2	3	
21	8684/13	76	1	2	2	2	2.5	1	1	1	2	A	A	A	1	2	
22	8837/13	57	1	1	1	2	2	3	2	3	4	P	A	A	3	6	
23	9063/13	54	2	2	1	1	3	1	1	2	3	A	A	A	2	4	
24	9074/13	46	2	1	1	2	6.5	1	1	1	3	A	A	A	3	5	
25	9077/13	37	1	1	1	2	2.5	1	1	2	2	P	A	A	2	3	
26	9119/13	65	2	2	1	1	6	1	1	2	2	A	A	A	1	2	
27	9142/13	48	1	1	1	1	4	1	1	2	3	P	A	A	2	4	
28	9215/13	48	1	1	2	2	5	1	1	2	3	P	A	A	2	4	
29	9631/13	56	2	2	2	3	7	1	1	3	3	P	A	A	2	4	
30	9634/13	75	1	1	1	1	2	1	1	2	3	P	A	A	2	4	
31	9741/13	65	1	1	1	3	2.5	1	1	2	2	P	A	A	2	3	
32	9969/13	57	1	1	1	2	10	5	1	2	3	P	A	A	3	5	
33	10137/13	55	2	2	1	2	4	1	1	2	3	P	A	P	2	4	
34	10252/13	39	2	1	1	1	5	1	1	2	3	P	A	A	2	4	
35	10478/13	42	2	1	2	2	2	1	1	3	3	A	A	A	1	3	
36	10711/13	56	1	1	1	1	4	4	2	3	3	P	A	A	2	4	

s.no	HPE no	Age	Sex	P/D	site	Gross	Size	Histological type	Lauren	Grade	Depth	LVI	PNI	Lymph	LN	stage	MUC1
37	10914/13	65	1	2	1	3	3	1	1	2	3	P	A	A	1	3	
38	11272/13	65	1	1	1	3	2.5	1	1	2	3	P	A	A	2	4	
39	297/14	66	1	1	1	4	3	3	2	3	3	p	A	A	1	3	
40	353/14	55	2	3	2	3	6	1	1	3	3	P	A	A	1	3	
41	713/14	63	2	2	1	3	4	2	1	3	2	A	A	A	2	3	
42	860/14	58	1	3	1	3	4	2	1	2	4	A	A	A	2	6	
43	862/14	66	1	1	1	1	4	3	2	2	1	A	A	A	1	1	
44	872/14	58	2	3	1	3	2	1	1	3	3	A	A	A	1	3	
45	993/14	54	1	1	1	2	4	1	1	1	4	P	P	P	2	6	
46	1106/14	40	1	2	2	3	7	2	1	2	3	A	A	A	1	3	
47	1249/14	62	1	1	1	4	6	3	2	3	3	A	A	A	1	3	
48	1364/14	26	1	1	1	1	3.5	1	1	2	3	P	A	A	3	5	
49	1585/14	65	1	5	1	3	5.5	1	1	2	2	A	A	P	2	3	
50	1805/14	60	2	1	2	3	8	5	1	1	3	A	A	A	1	3	
51	1810/14	40	1	1	3	3	6.5	2	1	2	4	P	P	A	2	6	
52	1910/14	65	2	1	5	2	6	1	1	2	3	A	A	A	2	4	
53	2020/14	50	2	1	1	2	2.5	4	2	2	3	A	A	A	2	4	
54	2024/14	20	1	5	1	3	3	2	1	3	3	A	A	A	2	4	
55	2379/14	40	1	5	1	2	9	1	1	1	3	A	A	A	1	3	_
56	2499/14	46	2	1	4	1	7	8	_	1	3	P	A	A	2	4	
57	2520/14	40	2	1	2	1	8	1	1	3	3	A	A	A	1	3	
58	2551/14	60	2	5	1	2	6	2	1	2	3	A	A	A	1	3	
59	3423/14	65	2	2	4	3	6	1	1	1	4	P	A	A	2	6	
60	3532/14	66	1	1	1	3	5	1	1	1	3	A	A	A	1	3	
61	3561/14	55	2	1	1	4	7	3	2	3	3	A	A	A	1	3	
62	3619/14	59	1	1	1	3	11	1	1	2	3	A	A	A	1	3	3+
63	3633/14	65	1	5	1	2	5	1	1	3	4	A	P	A	2	6	
64	3793/14	55	1	1	1	2	6	1	1	2	4	A	A	A	2	6	
65	3833/14	60	2	1	1	3	1	1	1	2	2	A	A	A	1	2	_
66	4145/14	45	1	5	1	3	4	1	1	2	4	P	P	P	2	6	
67	4409/14	41	1	2	2	2	7	4	2	3	3	A	A	A	1	3	
68	4618/14	62	1	1	1	2	4	1	1	2	4	A	A	A	1	4	2+
69	5723/14	57	2	1	1	3	3	4	2	3	2	A	A	A	1	2	
70	6098/14	75	1	1	1	2	4.5	1	1	2	3	A	A	A	1	3	
71	6451/14	64	1	3	1	2	2	4	2	3	3	A	A	A	1	3	
72	6461/14	36	1	1	1	3	5	1	1	3	3	A	P	P	2	4	1+

s.no	HPE no	Age	Sex	P/D	site	Gross	Size	Histological type	Lauren	Grade	Depth	LVI	PNI	Lymph	LN	stage	MUC1
73	6605/14	53	1	1	2	2	3	3	2	3	2	A	A	A	1	2	_
74	7311/14	55	1	2	4	2	4	1	1	2	3	A	A	A	1	3	2+
75	7350/14	51	1	1	3	1	5	3	2	3	3	A	A	A	2	4	3+
76	7546/14	71	2	2	1	3	9	1	1	3	3	A	A	A	1	3	2+
77	7675/14	50	1	1	1	3	5	1	1	2	3	A	A	A	2	4	3+
78	7765/14	45	1	1	1	2	9	1	1	2	3	A	A	A	1	3	_
79	8060/14	54	1	3	1	3	5	1	1	2	4	P	A	A	2	6	1+
80	8227/14	70	1	1	1	1	6	1	1	2	3	A	A	A	1	3	1+
81	8640/14	40	1	5	1	3	5	1	1	3	2	A	A	P	2	3	_
82	8676/14	57	1	1	1	2	10	2	1	3	3	P	A	A	1	3	2+
83	8753/14	30	2	2	1	2	11	1	1	3	3	P	A	P	2	4	1+
84	8969/14	70	1	1	1	2	3	1	1	2	3	P	A	A	2	4	2+
85	9068/14	51	1	1	1	4	5	5	1	2	2	A	A	A	1	2	_
86	9117/14	42	2	1	1	3	6	1	1	3	3	A	A	A	2	4	_
87	9186/14	50	1	2	2	4	5	4	2	3	1	A	A	A	1	1	
88	9322/14	60	1	1	1	3	5	4	2	3	3	A	A	A	2	4	
89	10095/14	65	1	1	1	2	3.5	1	1	2	2	A	A	A	1	2	1+
90	10421/14	55	2	2	1	4	3	1	1	2	3	P	A	P	2	4	_
91	10646/14	61	1	2	4	2	3	1	1	2	3	P	A	P	2	4	1+
92	10864/14	46	2	3	2	4	4	3	2	3	4	A	P	P	2	6	1+
93	10869/14	30	1	1	2	1	12	1	1	3	4	P	A	A	2	6	3+
94	11356/14	55	2	5	1	4	4	1	1	2	3	P	A	P	2	4	_
95	11361/14	84	1	1	1	2	4	1	1	3	3	P	A	P	2	4	1+
96	11421/14	70	1	1	2	3	7	1	1	1	3	A	A	A	2	4	_
97	11476/14	60	1	2	1	2	3.5	1	1	3	3	A	A	A	1	3	
98	11776/14	74	2	1	2	3	3	1	1	2	4	P	A	P	1	4	1+
99	11993/14	56	1	5	1	3	6	1	1	2	3	A	A	A	2	4	_
100	16/15	70	1	1	1	4	4	3	1	1	3	A	A	P	1	3	_
101	117/15	62	1	1	2	2	4.5	1	1	2	4	P	A	P	2	6	2+
102	206/15	33	1	1	1	3	4	1	1	2	3	A	P	P	1	3	_
103	603/15	60	1	3	1	3	10	1	1	2	2	P	P	A	1	2	1+
104	697/15	77	1	2	1	3	6	1	1	3	3	P	P	A	2	4	1+
105	1090/15	55	2	1	1	1	7	3	2	3	3	A	P	A	3	5	3+
106	1094/15	62	1	1	2	2	2	2	1	2	3	P	A	A	3	5	1+
107	1252/15	65	1	1	1	3	7	1	1	2	2	P	A	A	3	4	_
108	1628/15	43	1	1	2	2	6.5	1	1	2	3	P	A	P	3	5	2+

s.no	HPE no	Age	Sex	P/D	site	Gross	Size	Histological type	Lauren	Grade	Depth	LVI	PNI	Lymph	LN	stage	MUC1
109	1644/15	64	2	1	2	1	6.5	1	1	1	3	A	A	A	2	4	_
110	2288/15	48	1	1	1	3	7	5	1	1	3	P	A	P	1	3	1+
111	2555/15	30	2	2	1	2	3	2	1	3	4	P	P	P	2	6	3+
112	2635/15	76	2	2	4	3	6	1	1	3	4	P	P	P	2	6	_
113	3752/15	75	1	1	1	2	6.5	1	1	2	3	P	A	A	1	3	_
114	3833/15	45	1	1	1	3	7	1	1	2	2	A	A	A	1	2	_
115	3865/15	58	1	1	1	4	5	3	2	3	3	A	A	A	3	5	3+
116	4109/15	52	2	1	1	3	5	1	1	3	4	A	A	A	2	6	3+
117	4319/15	60	1	1	1	2	6	1	1	3	4	A	A	A	2	6	1+
118	4572/15	65	1	3	2	3	4	2	1	1	3	A	A	P	1	3	1+
119	4648/15	45	2	2	1	3	4	1	1	1	3	A	A	A	1	3	1+
120	4846/15	32	2	2	2	2	4	1	1	2	3	A	A	A	1	3	1+

KEY TO MASTER CHART

SEX

Male-1

Female-2

PROCEDURE DONE

Subtotal gastrectomy-1

Total gastrectomy-2

Palliative gastrectomy-3

Partial gastrectomy-4

Distal gastrectomy-5

SITE

Pyloro-antrum-1

Body-2

Fundus-3

OG junction-4

Cardia-5

GROSS(Bormann classification)

TYPE 1-1

TYPE 2-2

TYPE 3-3

TYPE 4-4

HISTOLOGICAL TYPE

Tubular-1

Papillary-2

Diffuse-3

Signet ring-4

Mucinous-5

Lymphoepithelial-6

Lymphoma-7

Squamous cell carcinoma-8

LAUREN'S classification

Intestinal type-1

Diffuse type-2

GRADING

G1-Well differentiated-1

G2-Moderately differentiated-2

G3-Poorly differentiated-3

DEPTH OF THE TUMOR

T1-1

T2-2

T3-3

T4-4

LYMPHNODE

N0-1

N1-2

N2-3

N3-4

STAGING

IA-1

IB-2

II-3

IIIA-4

IIIB-5

IV-6